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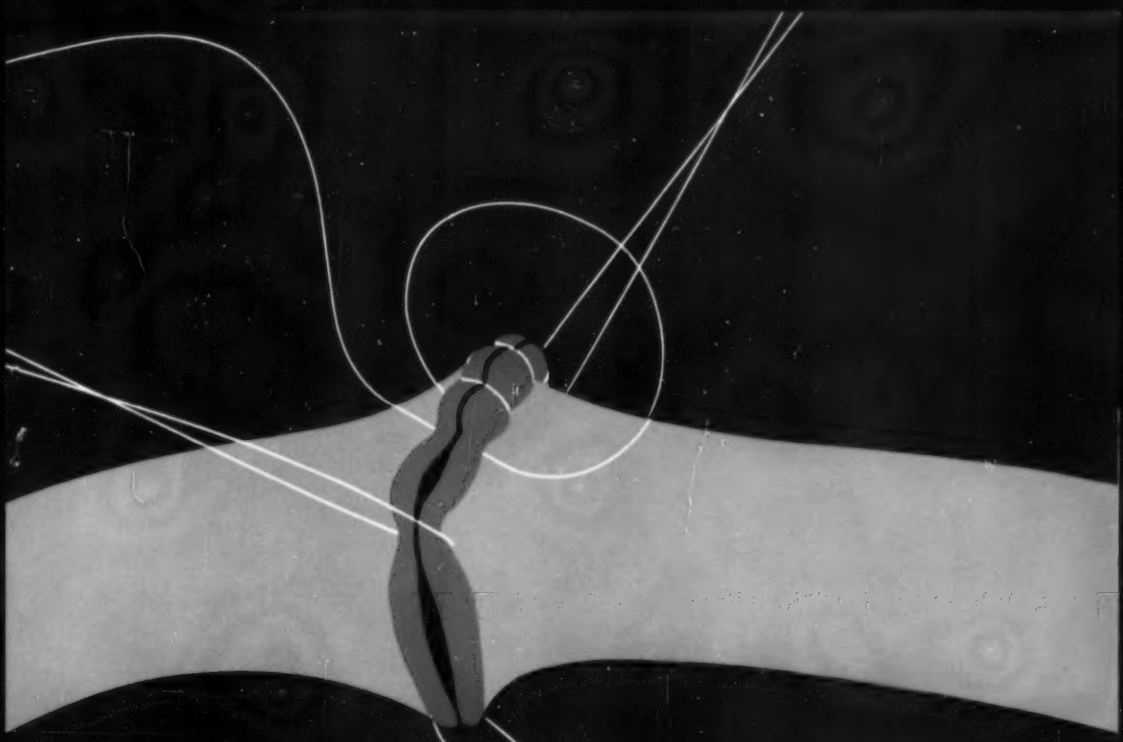

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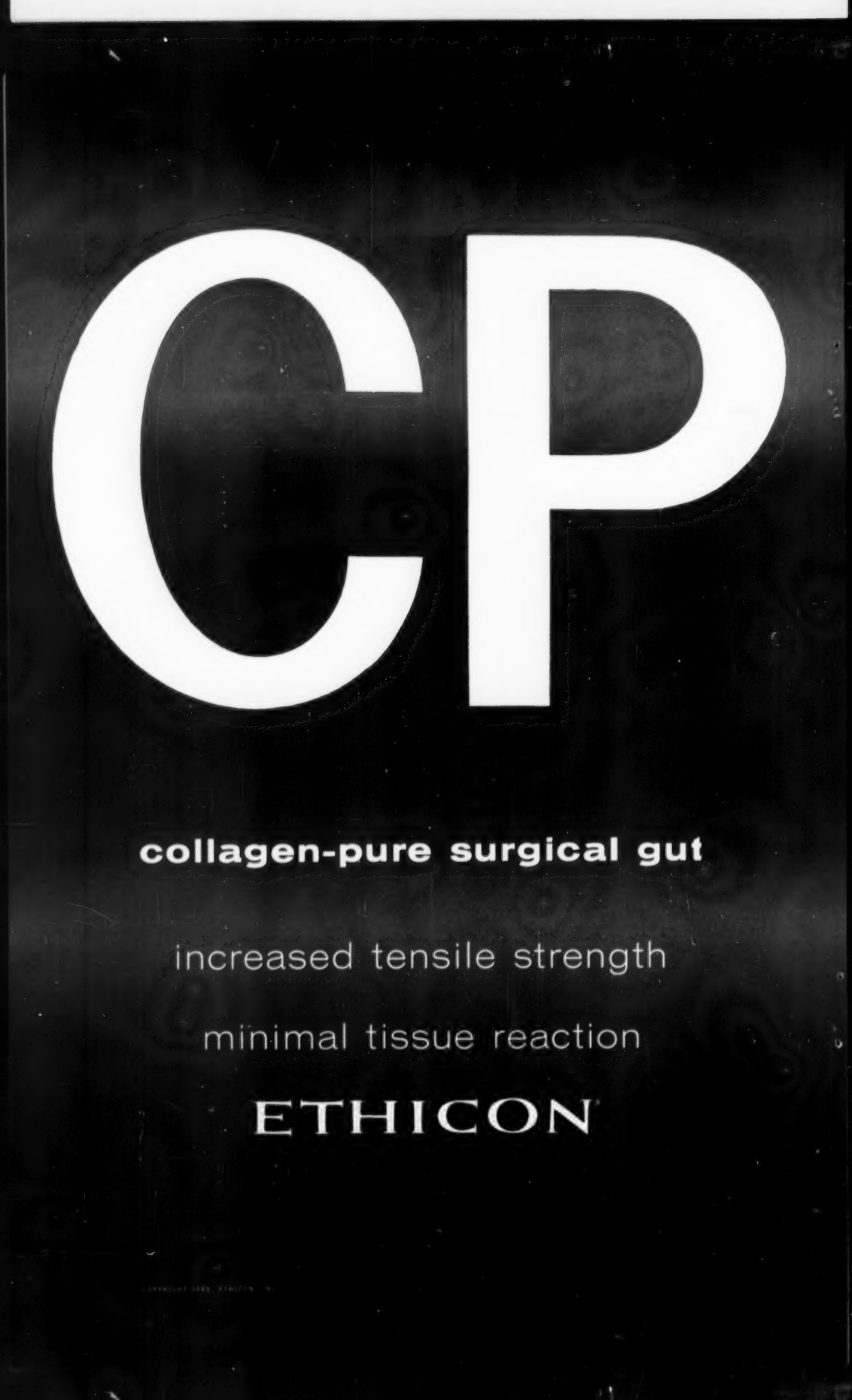
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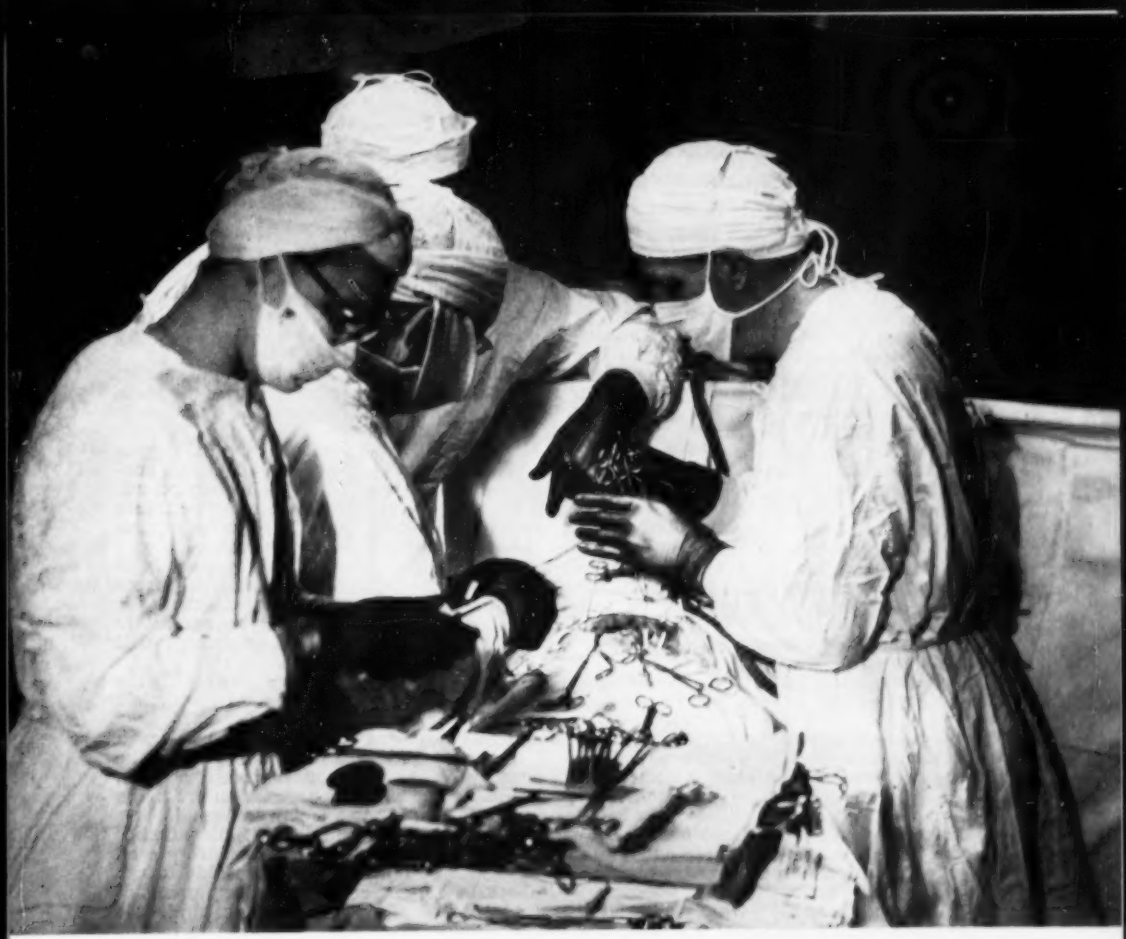

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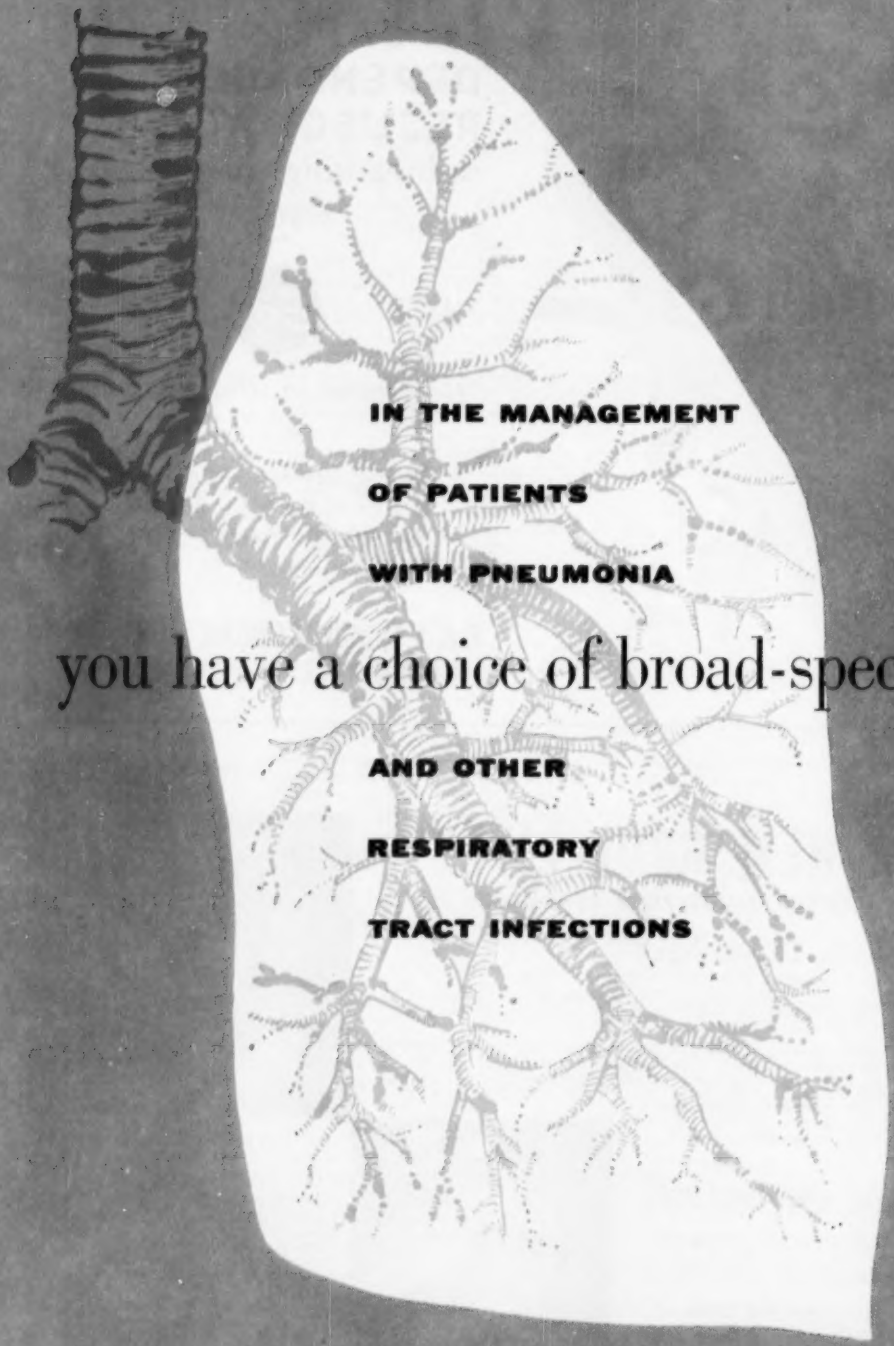

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Editorials

LETTER FROM THE EDITORS

THE MEMBERS of the Editorial Board hope that you will like the changes that have been made in the A. M. A. ARCHIVES OF SURGERY. The cover has been completely redesigned, and illustrations and space have been rearranged to present a maximum amount of material in the minimum compass compatible with good readability. Since it has been felt, in line with the policy of the Editorial Board to attempt to keep abreast of the major interests of all surgeons by such innovations as publication of Scientific Exhibits, editorials on timely topics, etc., some change in the physical form of the A. M. A. ARCHIVES OF SURGERY was in order. The editors accept a full share of responsibility for the changes. This is the second change in the format of the A. M. A. ARCHIVES OF SURGERY since its publication began, in 1920.

The editors will continue to do their part in selecting new, reliable, and informative material for the readers and in presenting it without undue delay, interestingly and with reasonable regard for economy of space, content, and arrangement.

WALTMAN WALTERS, M.D.
Chairman, Editorial Board

A SCIENTIFIC BASIS FOR THE SURGICAL TREATMENT OF CORONARY ARTERY DISEASE IN MAN

AFTER nearly a quarter century of relentless work in the surgical laboratory against overwhelming odds, due in part to the intrinsic nature of the problem and in part to misleading dogmas in existing medical information, Beck and associates have demonstrated beyond any reasonable doubt that alterations of blood flow with measurable dynamics can be produced in the myocardium of the dog, greatly reducing both the mortality and the myocardial destruction resulting from acute obstruction of a major coronary artery.

Some of the specific accomplishments in the surgical laboratory in the study of the coronary circulation, all firsts in the literature on this subject, by Dr. Claude S. Beck and associates are listed as follows:

1. Experimental studies began in 1932 to find direct surgical methods to improve collateral coronary circulation in obstructive diseases of coronary arteries.*

2. Demonstration of arterial extracardiac anastamoses, surgically produced of the caliber of large arterioles comparing in size to normal intercoronary anastamoses and available to enlarge to provide increasing collateral circulation to the myocardium in response to those factors causing enlargement of collaterals.[5]

3. Anatomical demonstration of enlargement of intercoronary anastamoses following chronic coronary arterial obstruction with measurement of size and study of histological character of the walls of these enlarged collaterals at their point of minimal cross-section.[5]

4. Measurement of hemodynamics of chronically occluded coronary arteries in the functioning heart with demonstration of increased peripheral coronary pressure

* References 1 and 2.

and backflow with method for determining quantitatively the sources of collateral flow to a given vessel.†

5. Observation of the resumption of contraction in myocardial muscle zones supplied by a chronically occluded coronary artery.[3]

6. Recognition of the function of collateral circulation in the heart with the acutely occluded coronary artery, i. e., preservation of life in the myocardial fibers and minimal function (electrocardiogram) until sufficient added collateral develops to permit resumption of contraction during systole. Also the development of criteria for obtaining quantitative data regarding minimal blood requirements to prevent infarction.‡

7. Demonstration of stimuli that cause enlargement of collateral arterial channels —acute arterial occlusion being most potent stimulus but that enlargement of collateral channels occurs in the absence of arterial obstruction as by abrasion of the epicardium, introduction of foreign material into the pericardium, arterialization of the coronary sinus or merely by exposing the heart surgically.§

8. Determination of a standard mortality (70%) rate for descending [a] ramus coronary artery (just distal to the septal artery) in laboratory dogs. A reduction in this mortality rate to 38% by previous abrasion, 27% by Beck No. 1 Operation and 9% by Beck No. 2 Operation. In all cases the amount of infarction being less than expected on the basis of the control studies but in keeping with the increased peripheral coronary pressure and backflow under these altered circumstances.‖

9. The application of this knowledge in devising surgical methods for the treatment of coronary disease in man begun in 1935 with modification of the operative procedure as new information is developed in the laboratory. The results have been gratifying to the independent observer.¶

Even if the laboratory work had no practical application in the treatment of disease in man, it would still be a scientific achievement of the first magnitude in the field of experimental cardiac pathology.

The fact that coronary disease in man has much in common with the laboratory studies and is one of the greatest unsolved medical problems of today, for which there is no other rational therapeutic approach, makes the achievement all the more significant.

Although the present status of the scientific knowledge that has been proved in the laboratory was strongly suggested as long as 15 years ago, the ultimate crucial evidence had to be accumulated by straightforward, well-controlled statistical methods involving (1) determination of mortality and infarct size resulting from a standard coronary artery obstruction in control and prepared animals and (2) blood flow studies into the ischemic zone of myocardium in control and prepared animals by the peripheral coronary artery pressure and retrograde coronary artery flow technique.

This program necessitated hundreds of experiments to prove each step of the present concept, not to mention time and effort spent in following false and unworkable hypotheses.

† References 6 and 7.

‡ References 5 and 12.

§ References 5, 8, and 11.

‖ References 8, 10, and 12.

¶ References 4, 9, and 12.

A bare skeleton of scientific facts have now been assembled to provide a sound basis for further study. The further questions that arise will easily keep a number of well-constituted research groups working for another quarter century trying to answer questions of pathological, physiological, and biochemical problems involved in the development and augmentation of collateral circulation in the myocardium of experimental animal and in furthering the application to the problem of coronary artery disease in man. It is hardly conceivable that our knowledge of the problem will remain static, now that the threshold has definitely been crossed.

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SURGICAL TREATMENT FOR ARTERIAL DISEASE

AS RECENTLY as thirty years ago the only surgical treatment for occlusive peripheral arterial disease was watchful expectancy until gangrene or infection of ischemic tissues developed; then high amputation of the extremity was performed without delay. Pioneer work on the surgical extirpation of aneurysms of the peripheral arteries and traumatic arteriovenous fistulas had been begun by Halsted and by Matas, but these operations were done with justifiable concern and considerable doubt as to the result. Aortic surgery was feared and avoided except for such crude procedures as insertion of wire into aneurysms.

During the past thirty years, and particularly since World War II, the surgical treatment of occlusive, degenerative, traumatic and congenital arterial disease has developed with increasing tempo and to an extraordinary degree. The early work of Leriche on periarterial stripping and the ramisectomy of Royal and Hunter led to the sympathetic ganglionectomy of Adson, which was found to correct arteriolar

spasm and improve impaired circulation, even when the cause was organic arterial occlusion. Improved technique has made regional sympathetic ganglionectomy a common therapeutic procedure with a mortality and morbidity rate of practically zero.

The value of the newly developed purified heparin in the prevention of arterial thrombosis was demonstrated by Gordon Murray and others, and this drug aided greatly in the successful employment of arterial embolectomy, thromboendarterectomy, and other reconstructive operations on the arterial system. Gross and others showed that, with careful techniques and the advances in safe thoracotomy, coarctation of the thoracic aorta could be corrected, and now the success of this operation is limited only by a too long delay before it is performed.

Autogenous grafts of segments of veins have been used successfully to bridge the gap in peripheral arteries caused by lacerating trauma or occluding disease. The first crude attempts to reinforce the weakened walls of abdominal aortic aneurysms with cellophane and fibroblastic stimulators have been replaced by resection of the entire aneurysm and insertion of an aortic homograft, which is actually dead tissue but which surprisingly resists mechanical stress for long periods and does not become the site of mural or occluding thrombosis. Similar aortic homografts have been used after resection of segments of the aorta occluded by atherosclerosis and thrombosis. More recently still, tubes made of certain plastic substances have been used instead of aortic homografts and with equal success.

The extraordinary expansion of surgical treatment for arterial disease during the past thirty years is the result of many factors. It has paralleled advances in general surgical techniques, improvements in anesthesiology, better supportive therapy, and better means for prevention of postoperative complications. The application of the new techniques has been possible because of more careful study of the patients, more precise diagnoses, and in many instances a knowledge of the exact nature and extent of the lesions gained through aortography and arteriography. However, the advances would not have been possible without the great technical ingenuity and untiring efforts in both laboratory and hospital operating rooms of some very active and able surgeons.

It is quite understandable, therefore, that a group of these surgeons have formed an organization for exchange of ideas and report of experimental and clinical investigations. In this issue of the A. M. A. ARCHIVES OF SURGERY will be found a group of papers presented before the second scientific medical meeting of the North American Chapter of the International Society of Angiology. In this group of papers will be found such interesting topics as "A Consideration of the Technic of Aortic Embolectomy," "Revascularization of the Ischemic Extremity," "Prolonged Experimental Occlusion of Thoracic Aorta During Hypothermia," "Replacement of Arterial Segments Utilizing Flexible Orlon Prostheses," and many other interesting papers dealing with the problems of improvement in circulation. It is anticipated that with the groups of able men interested in the field of vascular surgery and with their exchange of ideas, even greater and more rapid advances will be made in the future than have occurred in the past few years.

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REVASCULARIZATION OF THE ARTERIOSCLEROTIC EXTREMITY

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DEFINITION OF THE PROBLEM

WHEN AN extremity, predominantly the lower one, is suddenly or gradually deprived of its arterial blood supply, ischemia develops, which, depending on its extent, may cause death of the limb or functional disability or go unnoticed and remain subclinical. Since almost invariably even the subclinical forms progress toward manifest disease, early recognition and early treatment are essential. The problem then revolves around the finding of the cause of the ischemia, the localization of the process to a segment or to a regional vascular area, and the relief of this arterial stoppage. It seemed worth while to summarize the activities of our group along these lines. I shall attempt to present the philosophy underlying the activities of our peripheral vascular clinic, first started in 1926. Many of the thoughts expressed here were developed and reported in association with my former or present associates,* for whose help and collaboration sincere gratitude is expressed. Discussion will be limited here to the most frequent of peripheral vascular problems, namely, peripheral arteriosclerosis.

HEMODYNAMICS OF ISCHEMIA

It is a curious fact that clinical experience based on careful observations frequently antedates physiologic concepts. Pioneers like Leriche have been sorely plagued by the indifference or opposition of their colleagues when their proposed methods would not fit prevailing physiologic principles. Sympathectomy provides such an example, mostly because the four-footed animal under basal conditions showed only a transient increase in blood flow. Those of us who have long advocated this operation for peripheral vascular sclerosis have heard many an objection, consisting of absence of vasospasm in arteriosclerosis, return of vascular tone, and diversion of blood from muscle to skin after sympathectomy. In spite of marked clinical improvement, the experimental physiologist followed by many impressed clinicians could never see any logic in sympathetic denervation for peripheral vascular sclerosis.

Finally, however, the time has come to rationalize this procedure. Two important concepts with interlocking implications have come to the rescue and a brief allusion will be made to them here.

The concept of critical closing pressure has been enunciated by Burton and his associates.[1] They revived the old law of Laplace, dealing with the physical equilibrium of the vascular wall under the forces exerted by the pressure of the blood and the tension in the wall. Application of this law predicted that if the pressure within a small vessel fell below a certain critical value (the "critical closing pressure"), it would close actively and completely. With the help of flow-pressure curves this was found to be true in the isolated perfused rabbit ear, in the intact rabbit hind limb, and in the human arm.

The results of Burton's flow-pressure determinations are summarized as follows:

The critical closing pressure adds a new measure of vasomotor tone to the concept of vascular resistance. "Vascular spasm" simply means that the critical closing pressure

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Presidential address delivered before the North American Chapter, International Society of Angiology, San Francisco, June 19, 1954.

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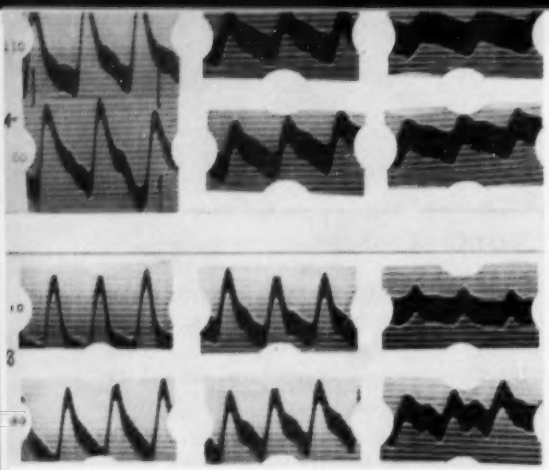


Fig. 1 (David W., aged 52).—Oscillometric tracings taken before and three months after a segmental resection of the superficial femoral artery in Hunter's canal. Note the high and steep curves 5 in. above the knee (*A*) which are lower after the occlusion has been relieved; *B*, note also the improved curves right above the knee and below the knee showing a shortened crest-line, an expression of the direct pulse wave. Curves obtained at 110 and 80 mm. Hg pressure with Dr. Carl Johnson's apparatus.

is higher than the available blood pressure. In conditions of high vasomotor tone, such as shock, vascular beds may be completely deprived of their circulation. Closure of the capillary bed might raise the critical closing pressure at arteriovenous shunts and result in their opening of the shunt. The level of blood pressure assumes a new importance in modifying the effect of vasomotor tone on circulation. In the arm of a human subject who had a critical closing pressure of 70 mm. Hg lowering the arterial pressure by 20 mm. Hg would result in a decrease of flow of 80%.

To apply these intriguing hemodynamic data to the problem, one may consider that sympathectomy raises the critical closing pressure in vessels below the occlusion by (1) reduction of vessel tone and (2) increasing intraluminal tension in providing more flow through collaterals. Thus, the trickle of nonpulsatile blood which maintains viability in some of these limbs is sufficient to prevent collapse of the vessel and subsequent thrombosis.

The second concept enunciated by Dornhorst and Sharpey-Schaefer [2] states that in ischemic limbs the collateral pathways cause increased vascular resistance which can be calculated by intra-arterial pressure measurements. Sympathectomy is capable of causing a considerable decrease in collateral resistance both in acute and chronic occlusions, although in 7 out of 10 cases the decrease was transient. It is not known how complete the sympathectomy was in these patients since, generally speaking, most sympathectomies affecting lower extremities are incomplete.[3]

Flasher and his associates [4] have recently stated their belief that sympathectomy does not increase the size of collaterals after ligation of a main artery nor does it raise the intraluminal pressure distal to the occlusion. They believe that in their experimental animals the rise in skin temperature was due to a shift of blood to the anteriovenous shunts of the toes.

Fig. 2.—Same patient as Figure 1. Femoral arteriogram with short, wide collaterals, delayed pulse at the ankle, walking ability of four blocks without pain. Note a large atheroma below the occlusion, causing stenosis and endangering the fate of the venous graft unless it is removed at operation. This is a Grade I arteriosclerosis; one and a half year follow-up with excellent results.

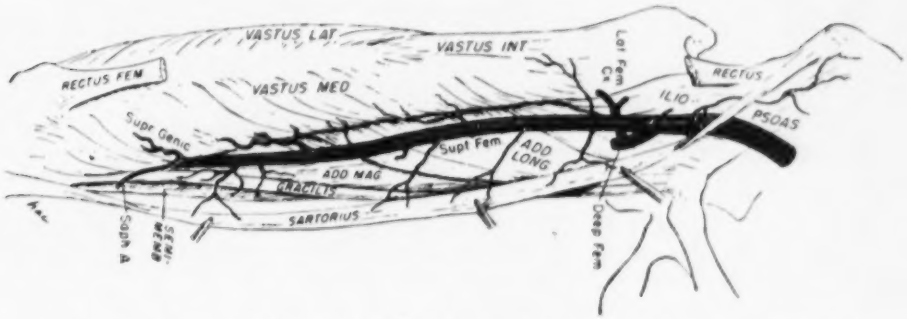


Fig. 3.—Muscle branches of the superficial femoral artery. The sartorious is entirely dependent on this vessel, the vastus medialis largely so. (From Edwards, E. A.: *Surg., Gynec. & Obst.* **97**:87, 1953; By permission of *Surgery, Gynecology and Obstetrics.*)

While anteriovenous shunts unquestionably open after sympathetic paralysis as demonstrated many years ago by Ford Hick and me with anteriovenous oxygen studies after sympathetic block,† I do not believe that in man the collateral supply is unaffected and that experimental conditions set up by the above-named authors can imitate the course of events in an acute occlusion.

Restoration of continuity by embolectomy, thromboarterectomy, or resection and vessel-graft clear the main pathway in an ischemic extremity but do not always restore the patency of important muscle branches; in fact, resection may destroy them. Such measures lower the pressure proximal to the occlusion (Figs. 1 and 2). Removal of a long segment of a closed superficial femoral artery can not revascularize individual muscles and may even aggravate their ischemia. A case of necrosis of the sartorius muscle was reported brought on by hematoma and infection but undoubtedly favored by absence of direct circulation to the muscle.[5] Sartorius claudication has been frequently observed by me after resection of the superficial femoral artery. An illustration borrowed from the work of Edwards[6] indicates the cause of such ischemia (Fig. 3).

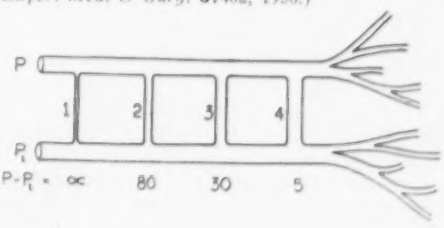
† Typical experiment: Three days after a left cervicodorsal sympathectomy the O_2 saturation in the left cubital vein rose from 42.5 to 83%. Right cubital vein showed an O_2 saturation of 73.6%. (Hick, F., and de Takats, G.: Unpublished experiments, 1936.)

A final consideration of the factors determining the efficiency of collateral circulation can be illustrated by Wiggers' diagram.[7] In Figure 4, two vessels, P and P_1 are shown to communicate through four channels of different sizes. Differential pressures of 5, 30, and 80 mm. of mercury are required to move blood through the collateral channels 4, 3, and 2, respectively, whereas an infinite pressure would be required to send blood through Channel 1. In order then for collateral channels to function, the head-pressure must be sufficiently maintained and the diameter of the collaterals must be as large as possible. In a sclerotic extremity relying for its viability on collaterals, a sudden fall in blood pressure and/or peripheral vasoconstriction due to shock or hemorrhage may bring on a critical state of circulation with acute massive thrombosis.

GRADES OF PERIPHERAL ARTERIOSCLEROSIS

In 1939, Beck, Roth, and I[9] graded peripheral vascular sclerotics into four

Fig. 4.—Diagram illustrating hydraulic principles which determine flow through side channels in tubes of different size. (From Wiggers, C. J.: *Exper. Med. & Surg.* **8**:402, 1950.)



groups since we felt that any result of treatment would have to be correlated with the stage of the disease in which it is undertaken. We have continued to use this grouping ever since, although obviously transitions and variations from one group to another frequently occur.

Group 1.—Warm extremities including toes, foot of normal color, no trophic changes, posterior tibial pulse present although sometimes weak or absent, claudication after two to six blocks, decrease of oscillations at ankle after rapid contraction of calf muscles.

An arteriogram of such a case reveals a short segmental stenosis of the superficial femoral or common iliac arteries. Weakness or absence of femoral pulse at the groin differentiates the two types of stenosis. Endarteriectomy of the common iliac artery for the upper type of stenosis and resection with end-to-end suture or venous graft for the lower stenosis have been the two methods of choice. Lumbar sympathectomy in a previously reported study has notably improved claudication in this group.[9] The big problem has always been the patency of the popliteal or subpopliteal segments, but the clinical appearance of the foot and the mildness of the claudication seem to be the best indication that blood flow through major channels is present below the obstruction. Leriche has astutely pointed out that the preservation of the fat pads in the toes and their normal color and warmth are the indices of a patent major arterial pathway distal to the segmental occlusion.[10]

Case 1.—E. T., a 46-year-old farmer (Case No. 55055, St. L. H.) entered St. Luke's Hospital on Jan. 16, 1954, complaining of gradually increasing claudication and numbness in the right foot and calf which finally ascended to the thigh and buttocks. He was unable to walk more than half of one block without having to stop. The right femoral artery did not pulsate, and the pulsations of the left one seemed diminished. Renal and cardiac function and eyegrounds showed no damage. Blood chemistry was normal, with the exception of a cholesterol level of 314 mg. per 100 cc. of blood. The heart and aorta were small on the chest film, but considerable calcification of the pulmonary vessels was noted. On the aortogram (Fig. 5), the right common iliac artery failed to visualize, but a faint trace of it was seen by retrograde filling below the origin of the internal iliac artery. There was a slight stenosis of the left common iliac artery, but this vessel filled well from above.

Through a midline laparotomy the aortic bifurcation was exposed. A Southwick clamp was placed proximal to the bifurcation and small rat-toothed clamps on the two external iliacs. A tremendous amount of atheromatous material was removed from the right common iliac, leaving very little media behind. On the left a short incision was made and a big saddle plaque was removed from the bifurcation. On resuturing the arterial incisions, both common iliacs pulsated well and there was good retrograde flow on both sides. A bilateral lumbar sympathectomy was done and the abdomen closed in layers. His postoperative course was uneventful. Both posterior tibial pulses, previously absent, were well palpable. Postoperatively he could walk eight blocks without pain. He can walk around his farm without cramping in his calves; pain in left buttocks and lower back are slightly present. He is maintained on a low-fat diet (one year follow-up).

Fig. 5 (Case 1, E. T.).—Aortogram. Width and contour of the aorta well maintained, but left iliac artery fails to visualize, whereas the right one is stenotic close to the bifurcation. On forward and retrograde femoral arteriograms no other occlusion was detected.

Fig. 6.—This film is rather hazy but shows the almost completely ocluded segment at the upper end of Hunter's canal. An ideal case for resection and direct anastomosis.

This is an excellent indication for a bilateral iliac endarteriectomy, which is preferable here to a resection of the bifurcation because of the good blood flow through the left common iliac and because the aorta itself was hardly involved.

Case 2.—E. J., a 49-year-old cotton planter (Case No. 57528, St. L. H.) entered the hospital on Feb. 25, 1954, complaining of numbness, tingling, and cramping of left calf after three to four blocks. Symptoms have been present since the fall of 1953. His cardiac and renal functional studies revealed nothing abnormal. Blood cholesterol was 314 mg. per 100 cc. His posterior tibial artery was pulseless and nodular, and oscillometric studies indicated marked decrease of oscillations below the left knee. On Feb. 26, 1954, a left lumbar sympathectomy was done between the iliac bifurcation and the diaphragm. At the same time a femoral arteriogram was performed, which revealed a sharply delineated arterial defect at the upper end of Hunter's canal, measuring about 1 cm. in length. Collateral circulation in the deep femoral was not too extensive (Fig. 6). Five days later the arterial occlusion was exposed. The artery seemed soft and pulsatile until the sharp edge of the adductor tendon, where it became hard, nodular, and stopped pulsating. A segment of little more than 1 cm. was resected and a mucoid granuloma reamed out from the proximal and distal segments so that a direct anastomosis could be made without an intervening graft. There was no tension on the suture line on 30 degree flexion of the knee, and the position was held for a week before full extension was permitted. Oscillometry before and after sympathectomy and after arterial reconstruction showed great improvement. The patient returned to Mississippi and writes that his walking ability has been restored.

This is the shortest segmental occlusion at the level of the adductor canal which my associates and I have seen; it was possible to reanastomose the proximal and distal segments without a graft. Longer follow-up is obviously desirable.

Group 2.—Cold foot when exposed to average room temperature. One foot is colder than the other without any obvious change in

Fig. 7 (Wm. S.).—Femoral arteriogram showing a bulbous obstruction at the site of a wide collateral coming from the profunda. The proximal end of the superficial femoral artery is not visible in the film, the large central vessel being the profunda. An endarteriectomy was done in 1951, but there was no evidence of patency three years later. Sympathectomy improved claudication from one to three blocks. Cold toes warmed up.

color. There are no trophic changes. The pedal pulses are absent although the oscillometer swings from 0.25 *to* 1 *cm. at the ankle.*

The needle of the oscillometer, however, makes a worm-like, slow excursion and not a rapid intense thrust which one associates with the patency of the main pathway. The slow oscillometric swing is due to a pulse coming through collaterals owing to a tortuous, elongated pathway and the increased resistance of the collateral pathway. Such a slow pulse wave can be demonstrably accelerated by sympathetic block and by sympathectomy, but claudication will not be improved by this operation; cyanosis disappears, and a warm dry foot results. Arteriograms indicate total occlusion and partial obliteration of long segments. Thus, the common and external iliac artery may be occluded, and the only distal filling becomes visible at the femoral bifurcation. Or the superficial femoral is occluded for some length but the profunda is patent. In fact, roughly speaking, this group is characterized by the patency of the profunda, a most important collateral channel (Fig. 7).

Sympathectomy is a most important procedure in such a situation, but extensive resections of the obliterated segments, combined with reaming out stenotic proximal and distal segments are worth trying. Endarteriectomy seems more useful for the iliac segment, whereas venous graft is preferable to replace the closed superficial femoral artery. Even so, the venous graft will close in about 30% of the cases ‡ when followed for one and one-half to three years. It should be remembered that a combination of iliac and superficial femoral closure aggravates the picture and that sympathectomy alone does not prevent obliteration of stenotic segments.

Group 3.—In such patients claudication occurs within half a block; the toes are shiny, atrophic, cold, and cyanotic, but the midportion of the foot and the heel are warm or can be warmed up by vasodilating procedures.

Small ulcers or patches of gangrene do occur. Pulses at the ankle are absent, and the aneroid type of oscillometer (Pachon, U. M. A.) does not show a swing. There is no rest pain, and prolonged bed rest together with prevention of heat dissipation by massive wraps of absorbent cotton bring about some improvement. The lesion here consists of a combination of closed major arterial path-

Fig. 8 (P. T., aged 61.).—Marked destruction of the femoropopliteal segment with some refilling at the popliteal bifurcation. Multiple segmental occlusions of the posterior tibial artery. Considerable effort at collateral development. Because of arteriolar involvement this patient had little increase in toe temperatures after sympathectomy and no increase in walking ability.

ways together with closure or damage to the terminal vascular bed including the digital arteries, arterioles, capillaries, and venules. Arteriolar sclerosis with capillary stasis dominates the picture and appears in hypertensives, in diabetics, and in patients with thromboangiitis obliterans or frostbite. Frost-

‡ Fontaine, R.; Riveaux, R.; Kim, M., and Keeny, R.: Le traitement chirurgical des oblitérations artérielles chroniques des membres, Paper Read before the First Congress of the European Society of Cardiovascular Surgery, Strasbourg, Oct. 5, 1952.

bite superimposed on arteriosclerosis or thromboangiitis obliterans is more apt to create such a lesion. Arteriograms should be used with great caution if at all in this group. More information may be gained by combining a test for reactive hyperemia with graded elevation.[11] "Direct surgery of arteriosclerosis"[5] does not seem applicable here although some authors have tried it. Sympathectomy may revascularize the toes, eliminate pain, and heal the ulcers but should always be preceded by a paravertebral sympathetic or a posterior tibial block (Fig. 8). Failure to warm the toes or a paradoxical drop in skin temperature either contraindicates sympathectomy or will have to be followed by high metatarsal amputation (Fig. 9). Arteriosclerotics occasionally, but not frequently, can be rehabilitated by a combination of lumbar sympathectomy and metatarsal amputation, a procedure more suitable for certain diabetics and patients suffering from Buerger's disease or frostbite.

Group 4.—In this terminal phase, the ischemia of certain areas such as the toes, foot or lower leg is manifested by severe color changes, such as cadaveric pallor or deep cyanosis, by areas of ulceration or gangrene, by marked edema often caused by a dependent, pain-relieving position during the night and by continuous rest pain, which even large doses of narcotics only partially alleviate.

Much ill-advised surgery is done at this stage, such as sympathectomies, toe amputations, and even endarteriectomies or vascular grafts, but they can not postpone an amputation at a proper level. This aspect of treatment is beyond the scope of the present discussion. Drug therapy and physical therapy may have to be used in the aged, the ones whose cardiovascular status is very poor, or those who refuse amputation. Rehabilitation of patients after major amputation is surprisingly successful, but the surgeon must take an active part in it. Sympathectomy of the opposite, less involved side has been our practice for many years; it may occasionally lower the level of amputation on the more involved side.[12]

SURGICAL PROCEDURES IN PERIPHERAL ARTERIOSCLEROSIS

Thrombectomy.—A great many patients with obliterating arteriosclerosis have a gradually increasing segmental stenosis, but as particularly stressed by Edwards,[13] "thrombosis is responsible for the major number of acute ischemic catastrophes in the arteriosclerotic limb." In earlier communications

Fig. 9 (G. I.).—High metatarsal amputation combined with lumbar sympathectomy was able to rehabilitate this 47-year-old salesman, who walks well on this short stump. Marked osteoporosis is due to a year of invalidism with lack of weight bearing.

on acute arterial occlusion,[14] I have always stressed the difficulty of differentiating an arterial embolus from an acute thrombosis but felt that thrombectomy was useless since the damaged wall would promptly reform the thrombus. This opinion needs modification because of the advent of two significant measures which favor patency after thrombectomy. First is the use of heparin for the sudden thrombotic occlusion. If given in proper dosage and with proper timing, it will arrest propagating thrombosis,[15] and if given

Fig. 10 (Wm. McE.).—A 62-year-old man, who developed a sudden arterial occlusion while on vacation in Mexico. He had previous coronary and deep venous thromboses. A long soft clot together with an atheromatous sequestrum was removed eight days later, with restoration of the lower femoral segment. Note the irregular defect above the complete occlusion and the faint refilling of the popliteal bifurcation.

intra-arterially proximal to the clot, may facilitate thrombolysis.[16] The second measure is endarteriectomy since experience has shown that the denuded media stripped of its atheromatous intima may remain patent for months and years. Thus, a thrombectomy undertaken proximal to an atheromatous occlusion should be followed by a thorough reaming out of the vessel and may well avert an acute ischemic catastrophe (Fig. 10).

Interestingly, organization of a thrombus does not take its usual course in a vessel with a thickened, hypoxic intima, and for this reason, thrombectomy should be considered as late as 8 to 14 days after acute occlusions. Resection of the thrombotic segment with its occluding atheroma followed by graft may be the optional procedure, but it is not practical in a case of popliteal and subpopliteal atheroma. Of six acute thrombotic occlusions, three were restored to patency.

Endarteriectomy.—The early suggestion of reaming out sclerotic arteries with catheters in amputation stumps to free collaterals above the ligature was followed by the ingenious method of J. Cid dos Santos who reamed out the inner core of an occluded atheromatous segment by the help of short incisions. Reboule introduced the longitudinal incision, which establishes a line of cleavage, leaves the adventitia and part of the atrophic media to form a new channel, and removes the organized clot, thickened intima, and atheromatous plaques in a well-defined line of cleavage. For the success of this procedure a normal pulsatile flow through the cleared segment is most essential. Systemic or regional heparinization after the operation was thought to be important, but in our experience it is only useful and safe during surgery, by irrigating both the proximal and distal clamped stumps continuously or intermittently. We have abandoned the use of postoperative heparinization except in the form of intraarterial injections in acute postoperative occlusions of the reamed segment. But most important is the state of the remaining lining of the newly constructed vessel. It must be smooth, glistening, translucent, not unlike the lining of an adventitious bursa. This line of cleavage is the result of a sequestration of a dead inner core of the artery from a vascular living arterial wall. Whether the ground substance with its toluidine blue staining exerts an anticoagulant or fibrinolytic action here is yet to be investigated, but

the fact remains that there is no fibrin and no adhesions between these two sections of the artery, and only the collaterals create an obstruction to pulling out long atheromatous, fibrous, and thrombotic strips from the occluded lumen.

I have limited the use of this method to the treatment of the stenotic or occluded common iliac artery; in three successive cases patency resulted with high oscillations on the thigh and return of femoral and posterior tibial pulses; on our own service, however, I have seen such vessels close at the completion of the operation for reasons which are not clear. However, the greatest problem is to know how far up and down the artery the operation is to be continued and how best to avoid the curling up of the sectioned inner core against the lumen.

The late results of endarteriectomy of the superficial femoral artery have been so poor that, at the advice of Fontaine and of dos Santos himself, I have not ever used it since autogenous or homologous vein grafts are preferable. Nor have we used endarteriectomy for the Leriche syndrome, although the reports of Wylie [17] and Freeman § are most encouraging.

Common iliac artery stenosis producing partial obstruction but allowing a pulsatile flow below the stenosis seems a debatable indication for endarteriectomy. Only recently in L. W., a 54-year-old patient whose aortograms were suggestive of a complete occlusion of both iliacs at the bifurcation, an incomplete obstruction was found with pulsatile flow below it. The artery was not opened, and the patient's spontaneous course will be carefully watched for signs of increasing obstruction. Of seven common iliac occlusions, two remained closed; but all three superficial femoral occlusions remained closed.

Vessel Graft.—The areas in which an excision of a totally occluded segment can be excised and the resulting defect bridged by an autogenous or homologous graft are at the aortic bifurcation, the iliofemoral segment, and the superficial femoral artery. We are satisfied at our institution that aortic thrombosis is best treated by excision and replacement with a frozen homologous aorta and that superficial femoral artery replacement can be successfully performed with autogenous saphenous veins, although we have also used homologous veins and, recently, I used a saphenous vein kept in the deep-freeze compartment for more than a month. The only requisite is the presence of a patent distal segment at the popliteal fossa with a demonstrable bifurcation of the posterior and anterior tibial arteries.

As so clearly stated by Leriche,[10] the absence of color and temperature changes and, particularly, the absence of atrophy or shrinkage of fat pads on the toes is a good indication that the main arterial pathways distal to the obstruction are patent. Nevertheless, a good angiogram is of great value in planning the operation or in abandoning the idea of restoring continuity. Out of eight patients with superficial femoral occlusion, six obtained a functioning graft.

There has been a rather justifiable aversion to the indiscriminate use of arteriograms,[18] and our attitude for many years has been to abstain from their use if its only object was to obtain a pretty picture. Certainly the patency of grafts, especially in the smaller, femoral segments, should not be demonstrated by postoperative arteriograms, since a closure of the graft may follow even after several years.[4] It is also true that the procedure should always be done by experienced personnel, not by frequently rotating residents, and that 10 mg. of heparin should be added to the opaque solution.‖ The concentration of colloidal iodine solution should not exceed 35% of femoral arteriograms, nor should the injection be repeated a second time within a few days. Aortograms are of course done with 70% solution, preferably with the use of intravenous thiopental (Pen-

§ Freeman, N. E.; Leeds, F. M., and Coelho, H. M.: Occlusion of Terminal Aorta and Common Iliac Arteries Treated by Thrombo-Endarterectomy, Paper read before Society for Vascular Surgery, June 20, 1954.

‖ dos Santos, J. C.: Personal communication to the author.

tothal) sodium or spinal anesthesia but not with local anesthesia.

DRUGS, DIETS, STEROLS

There has been an unprecedented amount of literature in the last few years on the effect of vasodilators, ganglionic depressants, and spasmolytic drugs employed to increase peripheral circulation. There are only a few drugs, notably heparin, procaine, 2-benzyl-4, 5-amidazoline hydrochloride (Priscoline), and histamine, which when given intra-arterially above the level of an acute obstruction really accomplish a regional vasodilation or prevent propagation of an arterial thrombus. One also sees occasionally a recanalization of an obstructed segment, but it may well be that the thrombus fragments, moves to the periphery, and is lysed by the natural defenses of the body, or that the artery stops hugging the clot and releases it to a lower level. The nature of these mechanisms is unclear, but in a recent highly provocative article Raymond Adams has made out a good case for a moving thrombus in apoplexy.[19]

For prolonged oral use, Roniacol, a derivative of nicotinic acid, has been in steady use in our clinic. A finger plethysmogram, taken with the Burch-Winsor apparatus, shows an increased pulse wave 20 minutes after the oral ingestion of 100 mg. of Roniacol (Fig. 11). This is a harmless nontoxic substance, and only a few people cannot tolerate it. There is no real evidence, however, that its prolonged use is capable of stabilizing blood flow at a higher level. Chemical sympathectomy with 10% phenol is another method which one can employ[20]—only in cases which ought to have sympathectomy but are too handicapped to tolerate it. Great caution should be used in its performance, and it is not to be used except in the lumbar segment.

Reduction of animal fat in the diet to 60 gm. a day has been employed in patients whose blood-cholesterol or cholesterol-phospholipid ratios are too high. Nelson Barker and his associates have practiced this method for many years, and our regionally sympathectomized patients are placed on such a diet with the hope of decelerating the progress of atheromatosis. I am not aware of any convincing proof that this is any help but have used the low-fat diet for many years.

The intriguing thought that estrogens may prevent atheroma formation because of the great increase in atheromatosis in men as compared with women before the menopause, in castrated women or menopausal women has created a great stir. However, Barr[21] pointed out that estrogen given to men with atheromatosis induces feminizing characteristics.

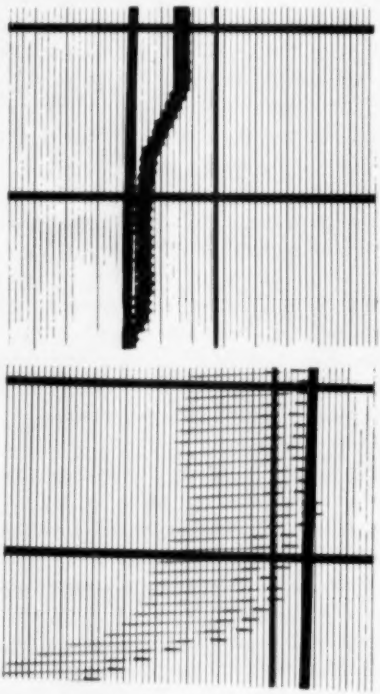


Fig. 11.—Plethysmographic tracing taken from right middle finger before and 30 minutes after 100 mg. of Roniacol taken by mouth. The Burch-Winsor apparatus was used.

Of the methods of physical therapy, only the oscillating bed and intermittent venous hyperemia apparatus have stayed in use. The former helps patients whose dependent edema is brought about by sitting day and night with feet hanging down to obtain relief

of pain. Actually a horizontal position with a few days of procaine and papaverine given intravenously or intra-arterially will accomplish as much. We studied the effects of intermittent venous hyperemia some years ago and found that the results had a great deal to do with the stage of the disease in which this ambulatory treatment was undertaken.[22] In the segmental occlusions today, one would prefer resection and venous grafting. In Groups 3 and 4 the treatment may often relieve pain, but ischemic neuritis or ascending lymphangitis is a contraindication. Generally speaking, I am using intermittent venous hyperemia less frequently than before because of the advent of more direct surgical methods for the early stages and because in the late stages, especially in the presence of arteriolar damage, it may do more harm than good.

COMMENT

The problem of revascularizing the arteriosclerotic extremity is intimately tied up with methods of prevention and methods of arresting the rate of progress of arteriosclerosis. No one can foretell the sudden occurrence of a stroke or of a coronary occlusion, but this threat need not hold us back from improving regional circulation in the extremities. Nevertheless, much present-day operative furor might be dampened if one had any kind of index of prognosis. Restoring the working ability and the economic efficiency of the patient, relieving him of his pain, and preventing a loss of limb are the objectives of surgical therapy, which should be intense and aggressive but well-timed. Ill-timed procedures in vascular surgery are numerous and should be discouraged.

Thus, in a case of acute arterial occlusion, the object is to save the limb by lumbar sympathectomy. Months later, when circulation is stable and the patient's walking ability is still severely limited, luminal restoration can be considered to improve claudication. This is a higher objective to shoot at but should be done only if the patient's improvement is at a standstill and if one is certain not to worsen circulation. I have made two short occlusions twice as long by having the implanted segment close, and such a possibility should always be considered.

The Table summarizes our present indications for the various surgical procedures. The number of cases is steadily increasing but 3- to 5-year follow-ups are not yet available. The use of plastic or metal substances for bridging arterial defects may revolutionize the whole field, but as of today, homologous and, preferably, autogenous material is still the method of choice.

Operations for Peripheral Vascular Sclerosis

Operation	Indications	Failures,* %
Sympathectomy	All acute and chronic arterial occlusions	25
Endarterlectomy	Iliac stenosis or occlusion	20
	Sup. femoral occlusion	50
Vein graft	Sup. femoral occlusion	30
Arterial graft	Saddle thrombus of aorta	10

* One to three year follow-up. Failure denotes mortality, loss of digits or limb, or closure of reopened segment.

SUMMARY

Revascularization of the ischemic extremity can be obtained by removal of clots, by reaming out an atheromatous vessel, by excision of the occluded segment followed by replacement and by sympathectomy. All these methods and their combinations have a proper place, but the indications depend on the regional appearance of the vascular tree, on the rate of progress of the disease, and on visceral circulatory status. Individual case reports are used to illustrate the problems encountered. Unlike the vascular repair in acute injuries, these procedures should always be weighed against the expected progress or standstill of arteriosclerosis. The Table indicates the present trends in our clinic, which are readily subject to modification.

122 S. Michigan Ave. (3).

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CLINICAL OBSERVATIONS ON VASOSENSORY INNERVATION OF LOWER EXTREMITY

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PERIPHERAL vascular sensibility has been a controversial subject since Leriche [1] first published his provocative clinical observations on arterectomy. Based on the clinical response of patients afflicted with obliterating arterial disease to excision of the thrombosed arterial segment, Leriche concluded that peripheral arterial tissue has a sensory innervation, that the neurons concerned with peripheral vascular sensibility course through the extremities within adventitia, and that these afferents traverse the extraspinal portion of the sympathetic nervous system before entering the spinal cord. Leriche has maintained consistently * that an inflamed artery is equivalent to an inflamed sensory nerve.

In 1922, Odermatt [4] had demonstrated pseudaffective pain reactions to distention of peripheral arteries and intra-arterial injection of irritating chemicals. Shortly thereafter, Friedrich,[5] Abrashanow,[6] and Schilf and Stahl [7] confirmed independently Odermatt's observations and also contended that many of the sensory neurons stimulated by the irritating intra-arterial injection passed centrally along the injected artery to traverse the lumbar sympathetic ganglia on their way to the spinal cord. Burget and Livingston,[8] Moore and Moore,[9] and Moore and Singleton [10] reached diametrically opposite conclusions. In their experimental animals, pseudaffective pain reactions to intra-arterial injections of irritants were eliminated only when the injected limbs had been rendered totally anesthetic by extensive spinal nerve section. In their animals, sympathetic ganglionectomy or arterial section proximal to the site of injection did not diminish the intensity of the pain reaction.

This peculiar experimental approach to the question of peripheral vascular sensibility is open to criticism. In the first place, it assumes as its basic premise that the mass indiscriminate irritation of sensory neurons as induced by an intra-arterial injection of an irritating chemical simulates the pathological painful entity of acute thromboarteritis. Secondly, it assumes that pseudaffective reactions of pain in the partially anesthetized experimental animal are reliable manifestations of all degrees and types of pain. Neither of these assumptions is tenable.

Additional experimental evidence which opposes or supports directly or inferentially the clinical concepts of Leriche are not too abundant. Wollard [11] describes in minute detail the innervation of peripheral vascular tissue by myelinated neurons. Kuntz and Farnsworth [12] have published histologic evidence of afferent neurons in peripheral sympathetic nerves. Unmyelinated fibers of class C (Gasser [13]) may play a role in the sensory innervation of the peripheral blood vessels. For instance, Heinbecker and others [14] were able to eliminate only 80 to 90% of the potential attributable to unmyelinated fibers of Class C in the saphenous nerve of the cat by severing that nerve's connection with the spinal cord. Within recent years, Threadgill [15] and Freeman, Shumacker, and coworkers [16] have demonstrated experimentally that vasosensory neurons from the hind limbs do traverse the lumbar sympathetic ganglia.

Actually, peripheral vascular sensibility is essentially a problem for the clinical inves-

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Presented at the Meeting of the North American Chapter of the International Society of Angiology, San Francisco, June 19, 1954.

* References 2 and 3.

tigator. Subjective responses to definite pathological processes and specific therapeutic procedures cannot be evaluated in the experimental animal. Is peripheral vascular tissue sensitive to noxious stimulation; does the resultant pain have characteristics which enable the physician to differentiate it from the subjective reaction to deprivation of blood, and are the neurons conconcerned with peripheral vasosensibility disposed anatomically in patterns identical with other peripheral afferents, or do they reach the dorsal spinal roots in some bizarre and as yet undetermined fashion? The following cases have been chosen for presentation be-

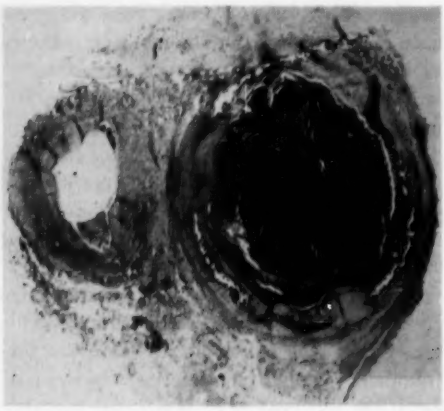

Fig. 1 (Case 1).—Low-power magnification of microscopic section of excised segment of adherent superficial femoral vein and recently thrombosed artery.

cause they answer partially these rhetorical questions, particularly insofar as the lower extremity is concerned.

Case 1.—L. B., a 48-year-old white man, had suffered from rheumatic heart disease since the age of 16. Three days prior to consultation he had been seized with severe pain in his left popliteal space plus coldness, numbness, and paresthesias of the foot. The foot immediately became very pale. Approximately 24 hours after this acute onset of ischemia, he began to feel a peculiar type of pain in the calf of the leg. At times the muscles felt as if they were tied into a knot; at times the calf felt as if it were going to burst open. This pain was present constantly; rest did not alleviate it, and it had become progressively more severe since its onset.

The man was in obvious distress. The left foot was palpably cold. It assumed a waxy pallor when elevated. The oscillometer registered no pulsation distal to the knee. The calf was flabby but exquisitely sensitive to manipulation. The popliteal and superficial femoral arteries were thrombosed, the latter up to the bifurcation of the common femoral. The patient complained bitterly when the thrombosed arteries were compressed.

Under regional infiltration anesthesia, the thrombosed femoral artery was exposed in Scarpa's triangle. It was inflamed and adherent to the contiguous superficial femoral vein and saphenous nerve. A 2-in. (5 cm.) segment of adherent artery, vein, and nerve was excised. The vein contained no thrombus. Leg pain disappeared at once, as if a sensory nerve had been severed. Squeezing the calf produced no discomfort, and the popliteal artery was no longer sensitive to pressure. There was no discernible improvement in peripheral circulation. The patient continued to complain of ischemic pain, coldness, and numbness in the foot for many weeks.

Figure 1 shows a microscopic section of the excised tissue. The pathologist's report follows:

"Sections show complete occlusion of the lumen of a large size artery by a thrombus mass composed in great part of red blood cells and fibrin. The intima and media show degenerative changes. The adventitia shows considerable round cell infiltration and edema. There is a diffuse regional cellulitis."

There is nothing unique about this particular case. Leriche and others have reported many similar experiences. For example, Freeman [17] has reported a series of 11 cases of intractable causalgic-like pain in the foot, the pain being a complicating factor in acute occlusion of the popliteal and superficial femoral arteries. In nine he was able to relieve the pain by resecting the thrombosed arterial segment. The interesting point in this particular case was the presence of two distinct types of pain in separate locations: ischemic pain in the foot and a visceral causalgic type of pain deeply situated in the calf. The latter disappeared at once when a segment of the proximally thrombosed arterial supply was excised, as if a sensory nerve had been sectioned; the former was not diminished at all by the procedure. Because of the inflammatory matting together of the contents of the subsartorial canal, one somatic sensory nerve was necessarily included in the excised block of tissue.

That was the saphenous nerve. However, this nerve is a cutaneous nerve which innervates skin between ankle and knee. It receives no filaments from the calf of the leg. Obviously, there must be a sensory innervation in the leg which is anatomically and functionally not part of its segmentally disposed somatic sensory innervation which, in the calf, is via the sciatic nerve. It might be contended that ligating the femoral vein improved the nutrition of the deep tissues in the calf and was responsible primarily for the symptomatic improvement. Discussion of this possibility will be deferred until after the following case has been considered.

CASE 2.—C. N., a 44-year-old white man, gave the following history. For the past six months his ability to walk had increasingly become impaired by pain in the calf of his left leg. He was now able to walk no farther than a block before he would have to stop and rest his leg. In addition he complained of a very cold and numb foot. Recently, painful ulceration had involved his toes. He was addicted to cigarettes.

The left foot was cyanotic, hyperhidrotic, and palpably cold. Several of the toes were ulcerated. Pulsation could be detected in the popliteal artery, but none could be felt in the dorsalis pedis or posterior tibial arteries. The oscillometer registered no pulsation in the region of the ankle. After administration of a low spinal anesthetic, skin temperatures of all the toes rose to vasodilatation levels in excess of 30 degrees, and oscillometric readings increased.

A lumbar sympathectomy was performed through an anterior, muscle-splitting retroperitoneal approach. Excised tissue was sent to the pathologist, who subsequently confirmed the removal of sympathetic ganglia and nerve. An excellent circulatory response was obtained. Immediately after surgery the foot and leg were palpably hot and dry.

The following morning the patient complained that during the preceding night the foot had very suddenly become cold, numb, and painful. Examination revealed that the previously patent popliteal and superficial femoral arteries were now thrombosed. The foot was mottled and palpably cold. Within the ensuing two days there developed, in addition to the ischemic pain in the foot, a peculiar type of pain in the calf of the leg. The pain was of an intense throbbing character; it was felt primarily deep in the calf but also radiated into the thigh along the femoral artery, and it was spasmodic. The deep tissues of the calf, the popliteal artery, and the superficial femoral artery were all sensitive to pressure.

Under regional infiltration anesthesia, the superficial femoral artery was exposed in Scarpa's triangle. It was found to be thrombosed up to its junction with the profunda femoris. The latter pulsated vigorously. On this occasion the thrombosed artery was isolated from the contiguous saphenous nerve and patent femoral vein, and a 2-in. (5 cm.) segment of the artery only was excised. As in the preceding case, the "vascular" pain and regional tenderness were relieved promptly. There was no improvement in peripheral circulation. Six weeks after arterectomy gangrenous ulceration of the foot had progressed to the point where it was necessary to amputate through the thigh.

Fig. 2 (Case 2).—Low-power magnification of microscopic section of excised segment of surgically isolated recently thrombosed superficial femoral artery.

Figure 2 shows a microscopic section of the excised tissue. As in the preceding situation, the pathologist reported the presence of a periarteritis.

These observations support the dictum of Leriche that an inflamed artery is the equivalent of an inflamed sensory nerve. In this instance, the only tissue removed was a segment of the thrombosed superficial femoral artery. Furthermore, the arterectomy was performed at a high level near the bifurcation of the common femoral, yet pain in the distal portion of the limb was thereby abolished. Clearly, vasosensory fibers must course

through the lower extremity along the walls of the major vessels. This case is unique in that "vascular" pain developed in a recently sympathectomized leg. The significance of this particular point will be considered after the following cases have been presented.

Case 3.—D. F., a 67-year-old white man, was seized with acute pain, coldness, and numbness in his right foot. He had never experienced intermittent claudication or other symptoms indicative of arterial insufficiency prior to the sudden onset of his present illness.

Examination 24 hours after appearance of symptoms confirmed the history of an acute deprivation of blood. The foot was cyanotic and palpably cold. The femoral artery pulsated; the popliteal, posterior tibial, and dorsalis pedis arteries did not. The oscillometer registered no pulsation in the distal portion of the leg.

Fig. 3 (Case 3).—Dissection of amputated leg to show recently thrombosed popliteal aneurysm. Distally, its branches were thrombosed. Proximally, the popliteal vein and artery were patent. The latter can be identified by the probe. The aneurysm was adherent to the sciatic nerve.

Procaine was injected paravertebrally into the lumbar sympathetic ganglia. Within 30 minutes the foot became warm; cyanosis disappeared, and pain was alleviated. Examination now revealed a large, pulsating, fusiform aneurysm involving the popliteal artery. Pulsation in the aneurysm had evidently been obliterated by spasm of the popliteal artery, which might have been induced by hemorrhage into the wall of the aneurysmal sac. Because of the incipient danger of thrombosis of the aneurysm, definitive surgery was advised, to be preceded by a lumbar sympathectomy. Unfortunately, operation was refused.

Five months later the patient was seen again during an acute attack of excruciating pain in the same foot. On this occasion, the ischemia had been precipitated by actual thrombosis of the aneurysm, which was now palpable as a firm, nonpulsating tumor. A lumbar sympathectomy was performed at once. Sympathetic ganglionectomy was confirmed by microscopic examination of the excised tissue. Peripheral circulation did not improve; the foot became massively gangrenous, and supracondylar thigh amputation was performed two weeks after the sympathectomy. Figure 3 shows the popliteal aneurysm exposed in the amputated leg.

Within three days, phantom limb pain appeared and became progressively severer. The pain was felt in the phantom calf and foot; it was causalgic, and when severest would be accompanied by clonic, uncontrollable, flail-like movements of the stump. During a particularly severe bout of phantom limb pain an attempt was made to arrest the convulsive motion of the stump by holding it down, whereupon the patient complained that the phantom foot and calf were being squeezed. Close questioning revealed that this squeezing sensation in the phantom was being elicited by pressure over the remnant of the superficial femoral artery.

Ten cubic centimeters of 2% procaine was infiltrated into the subsartorial canal around the artery. Within a few minutes all phantom limb pain disappeared and the stump became quiescent. Relief lasted for 24 hours. The injection was repeated, and transient relief of pain and cessation of the convulsive movement of the stump was again obtained. Under regional infiltration anesthesia, the remnant of the superficial femoral artery was exposed. It was occluded up to the profunda femoris. The latter pulsated vigorously. The superficial femoral artery was sectioned at its proximal limit of occlusion. Phantom limb pain was abolished and has not recurred. The patient uses a prosthesis and is comfortably active.

Case 4 (Mount Sinai Hospital, Cleveland; O. P. D. #38-475).—W. K., a 56-year-old white man, had been involved in an automobile accident eight years prior to his initial visit to the peripheral vascular clinic. Among other injuries he had sustained a compound fracture of the bones of the right leg. Gas gangrene necessitated amputation through the thigh. Phantom limb pain ensued and progressively became severer. When interviewed, he stated that the toes were being torn out of the foot, that the foot was on fire, and that he could not endure a prosthesis. He had previously undergone a resection

of the remnant of the sciatic nerve and a revision of the end of the severed femur, with no relief. He was thoroughly demoralized. Two per cent procaine was infiltrated around the femoral artery. Prompt alleviation of phantom limb pain was obtained, which lasted for 24 hours. Two subsequent injections yielded similar transient relief. Under regional infiltration anesthesia, the femoral artery was exposed in Scarpa's triangle. The artery pulsated down to its bifurcation. The occluded superficial femoral arterial remnant was sectioned just distal to the pulsating profunda. Relief of phantom limb pain was immediate and complete. After his discharge from the hospital, he began wearing his prosthesis and was able to work.

CASE 5 (Cleveland City Hospital; #279423).—J. M., a 67-year-old white man, had undergone a thigh amputation four months prior to his admission to the vascular surgery service. The amputation had been performed because of ischemic gangrene. After the amputation, he began to complain of phantom limb pain. It had become so severe that prefrontal lobotomy had been recommended by the consulting neuropsychiatrist.

When interviewed, the patient stated that the foot felt as if it were being squeezed by a tight shoe, that gravel was being ground into the sole of the foot, and that the foot was on fire. The stump itself was painful. The pain was worse at night, and he was about at his rope's end from pain and lack of sleep. The man was in obvious distress and in poor physical condition. It was decided that section of the occluded remnant of the superficial femoral artery in the stump should be tried. This was performed under regional infiltration anesthesia. Dramatic relief of phantom limb and stump pain was obtained.

Attempts to relieve phantom limb pain by peripheral neurotomy, segmental rhizotomy, and even spinothalamic tractotomy have been notoriously unsuccessful.[18] After reviewing over 100 cases, Bailey and Mosersch,[19] concluded that true causalgic phantom limb pain, in contradistinction to phantom limb sensation, cannot be explained on the basis of neuromata. Leriche believes that the sympathetic nervous system plays a fundamental role in the mechanism of phantom limb pain. Livingston [20] has reported a large series of cases of phantom limb pain wherein a single or multiple paravertebral injections of procaine into sympathetic ganglia aborted the disability. He has evolved an ingenious theory to explain his results. Temple Fay [21] has reported a very provocative case of phantom limb pain. A man afflicted with Buerger's disease had had his lower extremity amputated through the thigh. He developed excruciating phantom limb pain. The stump was rendered anesthetic by sciatic and femoral nerve section and injection of the dorsal roots, but the pain persisted. The lumbar sympathetic ganglia were injected with no relief of pain. (This is a particularly significant observation and will be discussed after the next case has been presented.) Phantom limb pain was not affected by spinal anesthesia until the level of anesthesia had been raised to the level of the second thoracic spinal segment. The man was cured by a high thoracic cordotomy. Three cases of thigh amputation have been included in this communication wherein section of the occluded remnant of the superficial femoral artery alleviated intractable and severe phantom limb pain. Inflammatory irritation of vasosensory fibers with projection of pain sensation into the missing distal portion of the extremity would appear to have been the mechanism responsible for the phantom limb pain in these particular cases. Although other mechanisms may initiate and maintain phantom limb pain, I believe that section of the major arterial remnant at the proximal limit of its occlusion should be the initial therapeutic approach in any case of phantom limb pain.

The final case to be presented is one of causalgic osteoporosis of the knee.

CASE 6.—B. B., a 50-year-old white woman, was seen 10 months after an accident in which the internal ligaments of her knee had been torn. She had fallen down a flight of stairs. After the injury, the knee became swollen and intensely painful. The swelling and pain had persisted for 10 months. The knee throbbed and burned constantly. It could not be moved either actively or passively because of associated painful muscle spasm. The foot was swollen, cold, and paresthetic. She had become a bed-ridden invalid, and it was supposed that she had become addicted to narcotics.

Examination revealed a very emotionally upset woman who was in obvious distress. The foot of the injured leg was cyanotic and palpably cold. It was edematous. Pulses were present. The knee joint was swollen but palpably hot and the skin was very hyperemic. The joint was fixed. Examination was almost impossible because of the intense pain.

Fig. 4 (Case 6).—X-ray of injured knee joint taken shortly after accident. The bone structure is normal.

Figure 4 is an x-ray of the knee taken shortly after the injury, and Figure 5 is the x-ray of the same knee 10 months later. The latter shows spotty decalcification which involves all the bones comprising the joint including the patella.

Procaine was infiltrated paravertebrally around the entire length of the sympathetic lumbar chain. Relief of pain and muscle spasm ensued, and it was now possible to passively flex the knee. Benefit lasted only a few hours, and so a lumbar sympathectomy using an anterior, muscle-splitting, retroperitoneally approach was performed. Excision of sympathetic ganglionic tissue and nerve was confirmed by microscopic examination. Pain was not relieved, nor was joint motion restored. A week later the common femoral artery was stripped of its adventitia. The following morning the patient voluntarily sat on the edge of her bed and flexed the knee without assistance. She no longer suffered pain. Narcotics were relinguished. Within a month she was walking with the assistance of a cane, and that, too, was discarded a short time later.

This last case may profitably be considered in conjunction with the other two in which "vascular" pain developed after a recent lumber sympathectomy. Here is a triad of essentially dissimilar clinical entities wherein lumbar sympathetic ganglionectomy either had not prevented or had failed to relieve pain of vascular origin, but wherein subsequent arterectomy, arterotomy, and periarterial sympathectomy respectively were followed by dramatic relief.

The irritated afferents apparently left the extremity with the femoral artery in these particular instances. However, if these vasosensory fibers were not destroyed when lumbar ganglia were excised, how then did they reach the spinal cord? The explanation may be found in the type of surgical approach utilized. In each instance the lumbar ganglia were exposed through an anterior, muscle-splitting, retroperitoneal approach, and it is

Fig. 5 (Case 6).—X-ray of same joint depicted in preceding figure taken 10 months following accident. Spotty decalcification involving all the bones of the knee including the patella was now present. Picture characteristic of causalgic osteoporosis.

impossible to secure the first lumbar ganglion and the cephalic portion of the lumbar sympathetic nerve and their connections with the preaortic plexus through this limited exposure.

This may be the essential clue to the anatomy of the extraspinal portion of the vasosensory innervation of the lower extremity. Conceivably, vasosensory neurons from the lower limb course along the iliac arteries and abdominal aorta, in the latter situation as part of the preaortic plexus. A variable number of peripheral vasosensory neurons may leave the plexus via its connections with lumbar ganglia. By traversing these ganglia and their connections with the first, second, and third lumbar spinal nerves, they reach and enter the spinal cord. (The first, second, and third lumbar nerves have sympathetic connections with the spinal cord via white rami communicantes.) Other peripheral vasosensory neurons may leave the preaortic plexus via its connections with the coeliac ganglion. By traversing this ganglion and the splanchnic nerves, along with other visceral afferents, they enter the spinal cord at various levels within the thorax.

This hypothesis is consistent with many clinical observations including those which have comprised the basis of this communication. For example it offers a reasonable explanation of Fay's aforementioned case wherein spinal anesthesia did not erase the perception of a painful lower limb phantom until the cord had been anesthetized up to the level of the second thoracic segment.

It might be concluded that if vascular pain in the leg is to be relieved consistently, a sympathectomy must include not only the ganglia connected with the first, second, and third lumbar spinal nerves but also the splanchnic nerves as well, which is essentially the subdiaphragmatic operation for essential hypertension. However, when the collateral circulation to a foot and leg is seriously impaired, the necessity for performing this extensive denervation must be weighed against the undesirability of stimulating the proximal portion of the limb and tissues outside the limb to compete with the ischemic distal portion for the more or less rigidly curtailed blood supply.†

The remaining question is concerned with the circumstances under which pain of vascular origin is encountered clinically. If vascular pain is conceived as being the peripheral equivalent of visceral pain, then a pheripheral artery becomes essentially a hollow viscus, and the same pathological entities that incite pain in a hollow viscus should induce pain in a peripheral artery. These would be inflammation and spasm. Direct irritation of vasosensory neurons by the chemical products of ischemia might also incite pain of vascular origin, particularly in highly vascularized tissue such as muscle. Thus, vascular pain might be a component of the symptom complex of intermittent claudication. The superior clinical results which high lumbar sympathectomy yields in properly selected cases of organic arterial disease of the leg ‡ might well reflect a vasosensory denervation and not the more extensive vasomotor denervation incident thereto.

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† References 22 and 23.

‡ References 24 and 25.

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BLOOD PRESSURE IN MINUTE VESSELS OF HUMAN SKIN

Clinical Estimation Made by the Method of Elevation and Reactive Hyperemia: II. Effects of Sympathectomy

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INTRODUCTION

THE PRONOUNCED cutaneous hyperemia upon release of a tourniquet has long been familiar to surgeons. This reaction, which is called reactive hyperemia, has been studied in detail by a number of workers, starting with Lister and including many of the outstanding names in vascular physiology. The period of hyperemia bears a definite relationship to the length of the circulatory arrest. Provided occlusion is not prolonged for more than a few minutes, the duration of the hyperemia is usually one-half to three-fourths that of the arrest.[1] It has been shown that the hyperemia represents the repayment of a blood flow debt which is built up during the period of arrest in the limb distal to the cuff.* The reaction is dependent upon accumulation of local metabolites during the period of arrest and upon the arterial pressure within the limb.[4] The intense cutaneous hyperemia is the result of dilatation of the minute vessels but it is not accompanied by a significant rise in skin temperature.

In 1933, Pickering[5] first suggested and standardized reactive hyperemia as a test of the circulation to extremities. More recently Di Palma and associates[6] described the reactive hyperemia ring test which also can be used as a test for the evaluation of skin circulation in obliterative vascular disorders. Winsor and his group[7] have described several plethysmographic techniques following occlusion of the arteries of extremities in the study of arterial insufficiency. These various techniques utilizing the principle of reactive hyperemia in the study of peripheral vascular insufficiency have been based mainly on the volume and rapidity of blood flow. Since capillaries are the portion of the circulatory system through which interchange of food and waste substances takes place and the capillary pressure is the most important factor in the transfer of foodstuffs from the blood stream to the tissues, it occurred to us that the pressure in the minute vessels of the skin might be of greater importance in the evaluation of peripheral vascular obliterative lesions than the volume flow.

METHOD

The filling pressure in the minute vessels of the skin of the foot has been estimated by a method of elevation and reactive hyperemia. Previous studies † have shown this test to be helpful in evaluating the degrees of arterial insufficiency, permitting a more accurate selection of patients to be treated by conservative methods, local amputations, or more radical procedures.

The test consists in raising the feet 65 cm. above the auricle for 2 minutes and then

Presented at the meeting of the North American Chapter of The International Society of Angiology, San Francisco, June 19, 1954.

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This work was carried out in part under contracts with the Veterans Administration, Research and Education Service (Nos. VAM-23388, VAM-23389, and V-1001M-3101).

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* References 2 and 3.

† References 8 and 9.

applying occlusive cuffs for 5 minutes. If within one minute after release of the cuffs reactive hyperemia does not appear, the feet are gradually lowered until flushing takes place and this level is noted. The appearance of reactive hyperemia has not only been measured by the appearance of color but also has been checked by the technique suggested by the work of Winsor[7]; that is, checking the increase in volume of a digit by the use of a plethysmographic cup, using the Burch-Winsor Plethysmograph. These two methods have been shown to agree quite closely. These studies have been carried out in the constant temperature room at a temperature of 24 C. with the patient under standard conditions of exposure.

The test has been repeated at intervals of several days in the same patient and the results have been found to be quite reproducible. The brachial blood pressure measured by the auscultatory method was carefully recorded. No changes in reactive hyperemia levels were noted which could be attributed to changes in blood pressure. Most of these patients have also been carefully evaluated by the usual clinical methods, including oscillometry, reflex vasodilatation test, sympathetic nerve block, peripheral nerve block, digital blood flow, digital plethysmography, and arteriography. The patients were tested before surgery; within the first 10 postoperative days, and again in the late postoperative period, up to one and one-half years.

The lumbar sympathectomies have been performed by the anterolateral retroperitoneal approach, taking the chain and ganglia from within the fibers of the diaphragmatic crus to a point over the promontory of the sacrum underlying the corresponding common iliac vein. Ventral rhizotomies have not been done.‡

The completeness of the sympathectomy was judged by the presence of increased warmth, dryness, and distention of the surface veins. In some of the cases, neurodermometry was utilized to map out the exact areas of sympathetic denervation, in others, by the lack of response on plethysmography to the startle reaction.

It is to be noted that this is a selected group because the majority of patients who have come to us with occlusion of major vessels and who need more than conservative care have been treated by endarterectomy rather than by sympathectomy.

RESULTS

Eighty-three lumbar sympathectomies were performed on 61 patients. A summary of the results is presented in the Table. In 60 of the 83 sympathectomized limbs, there was a significant rise in the filling pressure of the small blood vessels which was accompanied by definite clinical improvement. The rise in the filling pressure was usually greater in the late than in the early postoperative period. Of the 19 limbs which had no change in the filling pressures after sympathectomy, 13 already had levels which were maximal by this method of measurement. As would be expected, this included the groups in which abnormal vasoconstriction was prominent and organic obstruction minimal.

Effect of Sympathectomy on Level of Reactive Hyperemia

Condition	Improved, No.	Unchanged, No.	Decreased, No.
Vasomotor disturbance	1	10	0
Obliterative arterial disease			
Small vessels	30	3	0
Large vessels	25	5	4
Arterial obliteration with diabetes	4	1	0

In the group with obliterative arterial disease the results were much better in the patients with small vessel than in those with large vessel occlusion. Of the four patients who showed a decrease in the filling pressure of the minute vessels, two showed increased warmth after sympathectomy, and the temperature of the toes remained 2 to 4 degrees C. warmer on the sympathectomized side than on the control side on exposure to room temperature of 20 C. for one hour. In one there was an actual increase in blood flow to the digit as measured with a plethysmograph

‡ References 10 and 11.

and venous occlusion cuff at the ankle. Could it be that there was an actual increase in the total blood flow but that the wide-open arteriovenous shunts were short-circuiting the capillaries and smaller blood vessels? The clinical course of these last two patients was poor, both eventually having a supracondylar amputation.

COMMENT

The pressure in the proximal capillary and distal arteriole of the skin has been found by direct measurement to be approximately 32 mm. of mercury (about 45 cm. of water).[12] Capillary pressure varies widely and probably fluctuates in response to central pressure and local changes. It is interesting that the level which we found in our previous studies of 45 cm. as the level necessary to insure healing after transmetatarsal amputation corresponds closely to the level found by Landis by direct measurement of 32 mm. of mercury or 45 cm. of water. We feel, therefore, that this method gives us a good clinical estimation of the blood pressure in the minute vessels of the skin of the foot.

The purpose of sympathectomy in the treatment of peripheral vascular disease is manifestly to abolish the vasomotor tone in order to improve the circulation and to allow development of collateral blood vessels. The greater the impairment of circulation by vasoconstriction, the better are the results to be expected from sympathetic denervation. Most of the experimental evidence is in favor of the view that there is not a permanent loss of vascular tonus after sympathectomy in man. We have always felt that the admittedly good results following sympathectomy in well selected cases were primarily due to the stimulus for the development of collateral circulation. The local circulation also benefits from the fact that central and reflected impulses are no longer able to cause diminution of blood flow to a limb which already has a reduced blood supply. These studies are the first to show that after sympathectomy there is a definite increase in the pressure in the small blood vessels of the sympathectomized extremity. This increase is present in the immediate postoperative period when the removal of vasoconstrictor tonus is maximal. It is even greater in the late stages when the small arteries and arterioles have regained their intrinsic vascular tone. The delayed rise in pressure is probably dependent upon the development of collateral circulation.

CONCLUSIONS

In a series of 83 sympathectomies on 61 patients, there was a definite increase in 72% in the pressure in the small vessels of the sympathectomized extremity. On a clinical basis the results were best in the patients with abnormally increased vasomotor tone and no arterial obliteration, but this was not reflected in the reactive hyperemia levels as they were already maximal by this method of measurement. In the group with obliterative arterial disease, the patients with small artery occlusion did better than those with large artery occlusion.

These studies also suggest that this test is a simple, reliable, reproducible clinical method of evaluating peripheral arterial insufficiency and its response to treatment.

SUMMARY

The blood pressure in the minute vessels of the skin of the foot has been estimated by a method of elevation and reactive hyperemia. Previous studies in this laboratory have shown a prognostic relationship between this level and the healing of necrotic lesions of the foot. The present report deals with a series of 83 sympathectomies on 61 patients in whom the height at which reactive hyperemia appears has been measured before and after operation. These studies show that after operation there is in most of the cases a definite increase in the pressure in the small vessels of the sympathectomized extremity.

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METHOD OF BLOOD VESSEL ANASTOMOSIS BY MEANS OF METAL CLIPS

An Experimental Study

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IN JOINING together the tubular structures of the body, surgical craftsmanship approaches art. Successful anastomosis is based upon knowledge of the tube's structure, blood supply, mode of healing, and, above all, the properties of its contents. The means at hand are the smallest consideration.

The ideal vascular anastomosis represents a watertight junction sufficiently strong to resist lateral and longitudinal tension, whose inner surface offers neither mechanical nor biochemical inducement for thrombosis. The ultimate repair must not deform the lumen or hinder the growth of the vessel. In addition, the operation must be accomplished well within the safe time limit of occlusion for the area supplied by the vessel.

By the turn of the century, techniques necessary to the attainment of this aim, such as triangulation of the vessel and intima-to-intima approximation by means of everting sutures, had been devised.* However, the exacting and sometimes exasperating nature of blood vessel suture spurred investigation of simpler, more rapid methods at the very outset. The failure of devices such as external prothesis of ivory and magnesium, and intubation with paraffined tubes of various materials lay in the contradiction of one or more of the postulates of good anastomosis.[4]

Vascular surgery was nurtured in the experimental laboratory. Its techniques were displayed occasionally in the repair of peripheral vessels lacerated in accidents or battlefield injuries. It was not until the last decade that a real need for more rapid methods of anastomosis became apparent.

Since the early forties two major problems have engaged the interest of vascular surgeons: the direct surgery of occlusive arterial disease and the reconstruction of congenital vascular anomalies. Many of these procedures involve the great vessels, requiring their occlusion during operation for periods overlapping the limits of organ survival. It is obvious that in the solution of this problem, a faster method of anastomosis will be less perilous.

In this paper, a method of blood vessel anastomosis by means of stainless steel clips is presented. It is a more rapid technique than previous methods, while still adhering to the requirements of good anastomosis.

MATERIALS

V-shaped clips with a circle of spikes at either end grip the vessel wall and effect coaptation when compressed. The silver clips used initially proved unsatisfactory owing to lack of rigidity, dull spikes, and local reaction of the tissues.

At present the clips are made from stainless steel sheets, #302, cold-rolled, full temper, 0.005 in. thick. The dimensions of the present design make them satisfactory for use in dog aortas. A scale drawing of this clip is shown in Figure 1.

The clips are handmade; sheet steel is cut into strips of correct width. The sites of the spike holes are marked off along the strip and are punched through with a center punch. The strip is then turned and the punch inserted in the opposite direction to open out

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This investigation was supported by a grant from the Defense Research Board of Canada.

Presented at the meeting of the North American Chapter of the International Society of Angiology, San Francisco, June 19, 1954.

* References 1, 2, and 3.

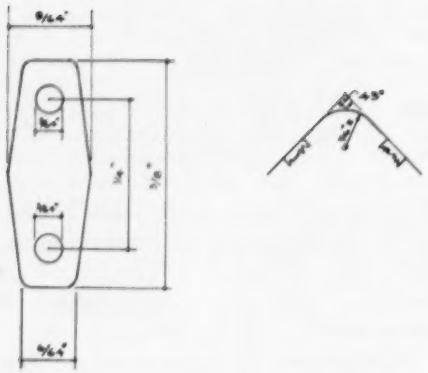


Fig. 1.—Diagram: stainless steel clip. A clip with these dimensions has been found suitable for use in the abdominal and thoracic aortas of dogs. Height of the circle of spikes, not indicated in the drawing, is approximately 0.025 in.

the points. The strip is now sectioned and cut to shape with scissors. The triangular sides enable the clip to grip the larger outer diameter of the everted vessel edge and the smaller inner circumference adjacent to the vessel wall without overlapping.

The clip is bent to shape over a brass form. One point is inserted into a hole at the side of the form, and the clip is bent at its exact center and in a plane at right angles to the axis between the points. Unless this is done precisely, the points will not coincide when the clip is compressed. The radius at the angle allows for the thickness of tissue held between the clip sides.

The clips are presently being applied with ordinary straight and curved hemostats. A coiled spring passing between the finger loops of the clamp serves to hold the clip firmly in place. The spring selected must hold the clip steady but not so strongly as to result in premature closure. In practice it is easy to select a spring of the correct strength. The clip is held in the terminal serration of the jaws. The clips may be picked up from a flat metal plate or from a simple rack as illustrated in Figure 2. Arrangements have been made with an instrument company † to manufacture clips, clip forceps, and clip rack.

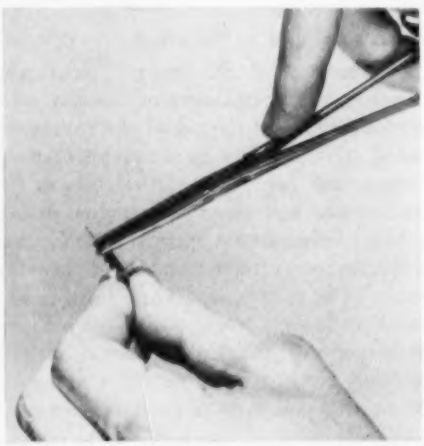
† Sklar Manufacturing Co., Long Island City, N. Y.

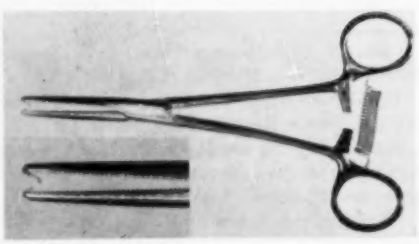
METHODS

An unselected group of mongrel dogs was used in these experiments. The procedures were carried out on the thoracic and abdominal aortas. The operations included longitudinal arteriotomy, and single and double transections with reanastomosis. Veterinary pentobarbital (Nembutal) given intravenously was used for anesthesia. Intratracheal tubes were inserted in all dogs undergoing intrathoracic procedures, and these were connected to a mechanical respirator.

The thoracic aorta was selected for use in the majority of operations. It was chosen because of its known friability, strong tendency to retract on section, brief period of safe occlusion, and the swift and certain outcome of a faulty anastomosis.

Fig. 2.—The upper photograph shows the method of loading the clip forceps from a simple slide rack. Below: a clip forceps with clip in place between the terminal serrations of the jaws. The spring between the finger loops is made from steel piano wire and may be easily replaced when necessary. Insert: detail of a clip held in the jaws of the clip forceps.





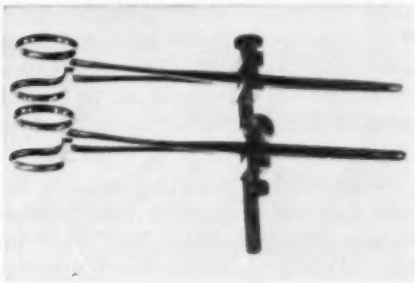


Fig. 3.—Photograph of a holding clamp designed for use with the aortic occlusion forceps. This holding clamp has excellent rigidity and is easy to adjust quickly because of the accessibility of controlling screws, all of which are on the same side.

The thoracic aorta was approached through the left chest wall. The incision overlay the seventh intercostal space. Ribs five, six, and seven were sectioned at their necks and the chest wall widely retracted.

The mediastinal pleura was incised longitudinally and the aorta dissected free.

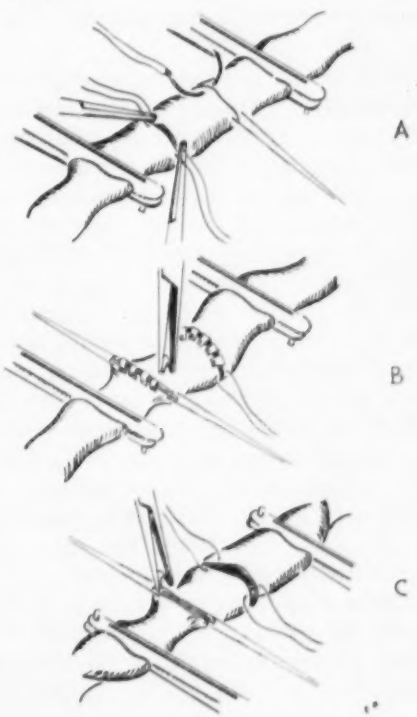
If a single transection was planned, two pairs of intercostal arteries were cut across. Three or four pairs must be severed in a double anastomosis.

Overmeticulous dissection of the adventitia should be avoided as it increases the friability of the vessel wall. A plane of cleavage just external to the adventitia seperates easily with gently dissection. The intercostal vessels should be dissected out with caution. They tear easily and the ensuing hemorrhage is quite out of proportion to their benign appearance. When the aortic segment is freed completely, it is occluded between Johns Hopkins Occlusion Clamps.† These are held at the desired distance by a holding clamp designed in this laboratory Figure 3. The use of such a clamp is considered essential in work on the thoracic aorta because of the considerable force of retraction and the necessity for performing the anastomosis by the clip method without tension. After occlusion, the vessel is transected between intercostals by clamping with another occlusion clamp and cutting the vessel through the central slot with a No. 11 Bard-Parker blade.

In performing a reanastomosis of a single transection, three traction sutures of No. 40 (surgical) cotton thread are placed at equidistant points around the vessel, using No. 14 Hagerdorn half-circle needles. The sutures should be placed about 2 mm. from the edge and at right angles to the vessel wall.

After placement of the two anterior sutures, the placement of the posterior suture is facilitated by rotating the holding clamp.

Fig. 4.—Diagramatic representation of reanastomosis of doubly transected thoracic aorta. *A*, The pair of sutures on the left have been passed and immediately clamped close to the aortic wall, serving to stabilize and orient the segment. On the right, the second pair of anterior traction sutures have been inserted. *B*, on the right, the edges of the aortic wall have been clipped together between the paired traction sutures. On the left, the clamps have been removed from the sutures and the row of clips is being completed by placing the last clip adjacent to the traction suture. *C*, the aorta has been rotated so that the posterior surface faces upwards, and the posterior traction sutures placed at each end of the segment. On the left, the clip line is begun just adjacent to the traction suture. Following completion of this row and the row opposite and parallel to it, the aorta is rotated back to its original position and the unclipped edges joined.



Paired traction sutures are pulled upward and outward, raising and everting the vessel edges (Fig. 4*B*). Clips are now applied beginning just beyond a traction suture and at intervals of 1 mm. until the opposing suture is reached. Three to four clips between sutures will usually suffice. Unequal eversion or failure to obtain level edges can usually be remedied by changing the amount and direction of traction on the sutures. Pressure with the fingertip beside an inverted edge serves to straighten it until the edges are stabilized by the application of one or two clips. By rotating the traction sutures and holding clamps, the two remaining sides are brought into view and clipped. If gaps remain at the site of the traction sutures, a clip is placed over the site and the suture cut off short. If no further gaps are apparent, the occluding clamps are removed. The distal clamp is removed first, followed by a gradual release of the proximal clamp.

The double transection and reanastomosis uses the same general technique as a single, with a few additional measures. The essential steps are shown diagrammatically (Figs. 4*A*, *B*, and *C*).

Four anterior traction sutures are placed; immediately after passing the first two sutures they are clamped near the vessel wall. This serves to fix the vessel segment in place and aids the accurate placement of the remaining two sutures. Immediately after placement these sutures are pulled taut and clips are applied. The forceps are now removed from the sutures at the opposite end which are put on traction and the vessel edges are clipped together. With the segment securely fixed by a row of clips at either end, the holding clamp is rotated and the posterior sutures are placed. The remaining sections are now clipped together in tandem, in the same manner as described for the single anastomosis. The procedure is accomplished in 10 to 15 minutes and is bloodless if the clips are applied properly. Slight hemorrhage may be controlled by finger pressure or suture of the bleeding point.

After the removal of the occlusion clamps, the anastomotic site should be cradled in the fingers as violent diaphragmatic and respiratory movements may occur at this point, placing a severe strain in the anastomotic site.

There are a few points regarding the application of the clips which bear mention. The clip should be closed only when the apex of the V abuts against the everted edge of the vessel. It is closed firmly without crushing the tissue. If an edge tends to fall away from its mate, it may be retrieved by placing one side of the clip firmly over the retracted edge. As the clip is rotated to encompass to opposing side, the retracted edge is brought up into correct alignment.

On completion of the anastomosis, the mediastinal pleura and thoracotomy wounds are closed.

Longitudinal arteriotomy wounds are repaired by placement of clips between guide sutures.

A reliable prognosis following these operations may be gained from three observations. If the sphincter ani is tight, knee jerks present, and femoral pulsations strong, complete recovery is in order.

RESULTS AND OBSERVATIONS

1. *Arteriotomy and Intimectomy.*— The results in this small series are shown in Table 1. These procedures were performed in connection with another project and are included to demonstrate the feasibility of closure of such wounds by means of clips. This is actually extremely easy.

The silver clips used earlier in the series tended to promote excessive fibrosis and stenosis. It has been previously pointed out that longitudinal closure of blood vessels is usually followed by some degree of stenosis of the vessel.[8] The mode of healing is similar to that which will be described for the vessel transections.

2. *Single Transection and Reanastomosis.* —The results of this series are summarized in Table 2. In one of these procedures the abdominal aorta was utilized. The remainder

TABLE 1.—*Longitudinal Arteriotomy and Intimectomy*

Dog No.	Vessel	Type of Clips	Time Aortic Occlusion, Min.	Complications	Post-Operative Life, Days	Fate of Animal	Condition of Anastomosis
26	Abdominal aorta	Silver	20	Stenosis and occlusion of aorta	34	Died	Periaortic fibrosis and fibrosis of the suture line reduced diameter of lumen to 1 mm.
83	Thoracic aorta	Stainless steel	18	None	94	Killed	Minimal constriction of lumen clip line perfectly healed
47	Thoracic aorta	Stainless steel	21	Overheparinization and subcutaneous hemorrhage	⅝	Died	Aneurysmal dilation of intimectomized area
98	Thoracic aorta	Stainless steel	17	None	..	Surviving	.....
85	Thoracic aorta	Stainless steel	18	U. R. I. pneumonia	1	Died	Aneurysmal dilation of intimectomy site; clip line healing
59	Thoracic aorta	Stainless steel	20	Empyema	4	Died	Aneurysmal dilation of intimectomy site

TABLE 2.—*Single Transection and Reanastomosis*

Dog No.	Vessel	Type of Clips	Time Aortic Occlusion, Min.	Complications	Post-Operative Life, Days	Fate of Animal	Condition of Anastomosis
55	Abdominal aorta	Silver	14	None	165	Killed	Aortogram shows no constriction of lumen; anastomosis well healed with smooth intimal surface
512	Thoracic aorta	Silver	18	Spastic paralysis	11	Killed	Aortogram shows no constriction; anastomotic line smooth
43	Thoracic aorta	Silver	11	None	120	Killed	Aortogram shows cone-like constriction, periaortic fibrosis; pleura contracted across anastomotic site
94	Thoracic aorta	Silver	18	Spastic paralysis	5	Killed	Mural thrombus propagating from improperly placed clips; lumen reduced by half
40	Thoracic aorta	Stainless steel	11	None	129	Killed	Aortogram shows slight constriction of lumen; minimal fibrosis around anastomosis; intimal surface smooth
62	Thoracic aorta	Stainless steel	14	Shock	⅛	Died	Some separation of intima; anastomosis otherwise intact
12	Thoracic aorta	Stainless steel	8	None	66	Killed	Aortogram shows slight constriction of lumen; pleura tightly contracted; minimal perianastomotic fibrosis; intimal surface smooth
72	Thoracic aorta	Stainless steel	8	None	67	Killed	Slight constriction of lumen on aortogram; marked perianastomotic fibrosis; intimal gap 1 cm. long and 5 mm. wide at center of ovoid shape covered by endothelium
13	Thoracic aorta	Stainless steel	8	None	78	Killed	Aortogram shows slight constriction; slight perianastomotic fibrosis; intima smooth
90	Thoracic aorta	Stainless steel	7	None	91	Surviving	.....

TABLE 3.—*Double Transection and Reanastomosis*

Dog No.	Time of Occlusion, Min.	Complications	Post-operative Life, Days	Fate of Animal	Condition of Anastomosis
36	30	Spastic paralysis	3	Died	Anastomosis intact; intima clear
27	16	Overdose of anesthetic	1	Died	Anastomosis intact; intima clear
24	15	Overdose of anesthetic	1	Died	Anastomosis intact; intima clear
99	22	None	28	Killed	Aortogram shows marked constriction; considerable perianastomotic fibrosis; small aorta; relatively large clips; intima smooth
72	18	None	46	Surviving	.....
65	16	Weakness of hindlimbs; chest wall infection	14	Died	No constriction of anastomosis; intima clear
53	13	None	23	Killed	Aortogram shows no constriction of lumen; no perianastomotic fibrosis
81	16	Died on table; technical error	..	Died	.....
62	17	None	37	Surviving	.....
84	12½	None	28	Surviving	.....
26	17	Heart failure and pleural effusion	6	Died	Anastomosis intact; intima clear
25	20	None	22	Surviving	.....
22	17	None	21	Surviving	.....
47	16	None	18	Surviving	.....
30	11	None	17	Surviving	.....
18	10½	None	16	Surviving	.....
67	8½	None	16	Surviving	.....
74	8½	None	16	Surviving	.....

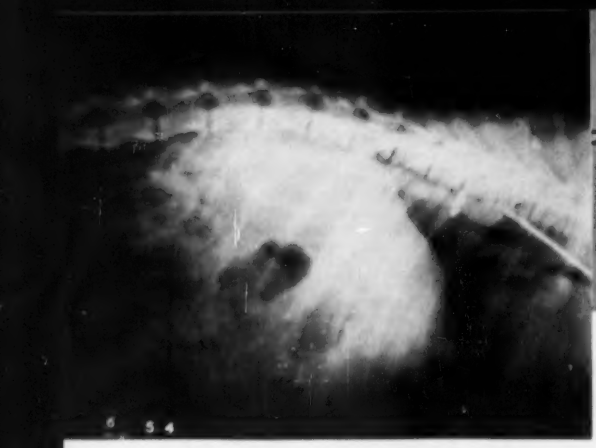


Fig. 5 (Dog 13).—Aortogram: 78th postoperative day. A tapering constriction of the lumen is seen proximal to the suture line. Contraction of a tightly sutured pleura with anterior-posterior compression of the aorta is the probable cause of this phenomenon.

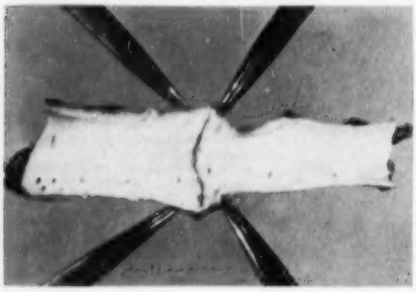


Fig. 6 (Dog 13).—Photograph of a gross specimen of the anastomosis whose aortogram is shown in Figure 5. The lumen is clear of thrombi and the anastomotic line appears as a transverse linear depression.

were performed on the thoracic aorta. Silver clips were employed in the abdominal aorta and the first two thoracic procedures.

Two of the 10 dogs developed spastic paralysis and were killed on the 5th and

Fig. 7 (Dog 53).—Aortogram: 23d postoperative day. Slight local constriction of the lumen has occurred at the clip line. The pleura was left unsutured in this dog.

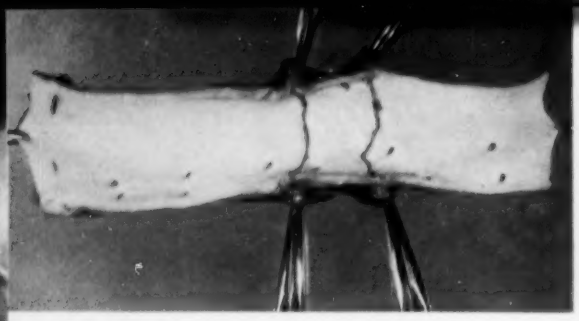
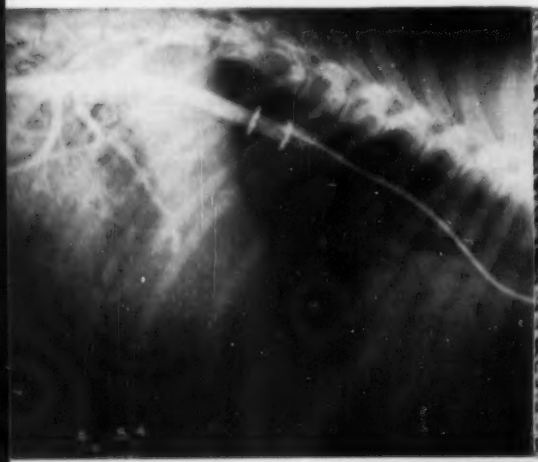


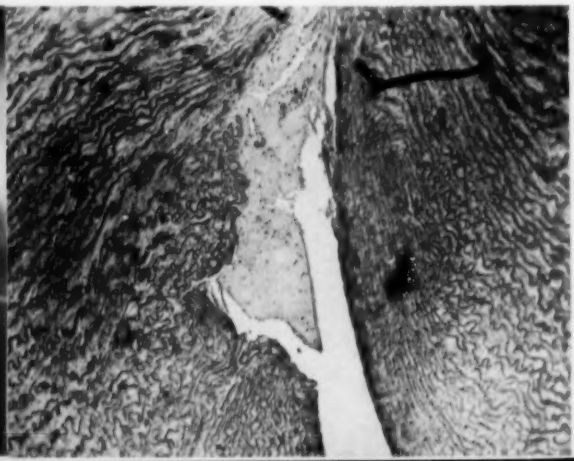
Fig. 8 (Dog 53).—Photograph: gross specimen of the double anastomosis in dog whose aortogram is seen in Figure 7. The complete eversion of the aortic wall by the clips is demonstrated on the cut edge. A layer of fibrous tissue on the external surface beyond the clip line on either side invests the anastomotic lines and bridges the interval between them.

11th days. One dog died of shock in the postoperative period. The remainder, save one which survives, were killed at intervals. Aortograms performed on the dog prior to sacrifice showed slight constriction at the anastomotic site in most of the animals. In Figures 5 and 6 an aortogram and gross condition of the anastomosis are shown.

The only case of a thrombosis in the lumen occurred in dog No. 94, in whom silver clips were used. After anastomosis, a short longitudinal tear was seen to extend from the clip line, and a clip was placed over it. It appears that the dull point of the silver clip failed to grip one side of the tear and, in consequence, the clip was rotated into the lumen where a thrombus developed around it.

Fig. 9 (Dog 26).—Photomicrograph of the anastomosis of the thoracic aorta six days postoperatively, with Weigert, hematoxylin, and van Gieson stains; × 40. Before viewing this section and those in the following figures, it should be pointed out that the clips are removed prior to embedding. The removal of this mechanical support plus the shrinkage incident to the histological section produces separation of the everted aortic wall which is an artifact. The fibrinous deposit at the apex of the intimal cleft is shown with organization in progress.





3. *Double Transection and Reanastomosis.*—The results of this series are summarized in Table 3.

There were 18 dogs in this series. Of the six deaths, one occurred on the table as a result of technical error. The remaining deaths occurred postoperatively. Two dogs are believed to have died from an overdose of anesthetic. The occlusion times in these animals were 15 and 16 minutes. One dog died five days postoperatively as a result of heart failure with pleural effusion. Another dog died after three days of unknown causes.

The remaining dog developed a chest wall infection and died 14 days postoperatively. In all postoperative deaths, the anastomoses were intact and the lumens clear. Two animals were killed on the 38th and 23d days postoperatively. The aortogram and gross appearance of anastomosis in Dog 53 are shown in Figures 7 and 8. The remaining dogs have survived without incident. The average occlusion time was 15 minutes for this series.

HEALING OF TRANSECTIONS AND REANASTOMOSIS

On gross inspection a definite fibrous layer appears surrounding and overlying the clip line by the second postoperative week. The lumen shows a circular depression at the anastomotic site which is almost obliterated by the end of the fourth month. The clips remain invisible from the intimal surface. The adventitia of the vessel at the operative site is thickened as a result of the periaortic fibrosis. This was much more obvious after the use of silver clips. The sutured pleura may occasionally compress or displace the aorta if it contracts on healing.

Microscopic sections at various stages of the healing process allow the sequence of events to be reconstructed as follows. Immediately postoperatively the cleft in the intimal surface is filled in with fibrin. The exudate from the surrounding area coats the external surface of the vessel. The edges held by the clips begin within two to three

Fig. 10 (Dog 53).—Photomicrograph of the anastomosis in the thoracic aorta 23d postoperative day, Weigert, Hematoxylin, and Van Gieson stains × 20. This is the same dog whose aortogram and gross specimen appears in Figures 6 and 7. The everted aortic wall shows slight pressure necrosis. The apex of the anastomotic line has been filled in and bridged in with fibrous tissue. The dense connective tissue seen on either side of the section previously surrounded the clip as shown grossly in Figure 8.

days to show signs of pressure necrosis (thinning of elastic fiber and smooth muscle bundles—pallid staining and pyknosis of nuclei). Within three to four days the fibrinous coats on the internal and external surfaces are invaded by a vascular granulation tissue, which is converted gradually over a two-week period into fibrous tissue. The main bulk of the tissue binding the vessel together appears on its external surface. The wedge-shaped granulation tissue in the intimal cleft appears as a fine network between the everted edges. Endothelial cells cover the granulation tissue-fibrin mass within

Fig. 11 (Dog 99).—Photomicrograph of the anastomosis in the thoracic aorta 38th postoperative day, Weigert, Hematoxylin, Van Gieson stains; × 40. This section passes through the plane of a cotton traction suture seen crossing the everted aortic wall. The underlying intimal cleft has been bridged over by fibrous tissue, and strands of connective tissue are seen between the everted edges above the suture.

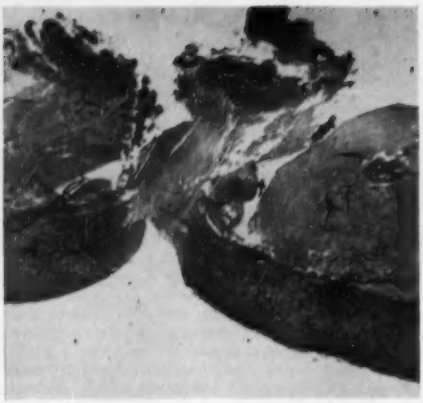
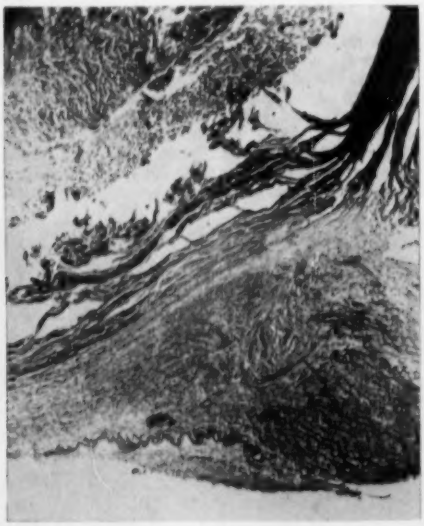


Fig. 12 (Dog 40).—Photomicrograph of the anastomosis in the thoracic aorta 129th postoperative day, with Weigert, Hematoxylin, and van Gieson stains; × 20. Healing is almost complete. The everted aortic edges have fused, and the media is replaced by a band of fibrous tissue. A mass of fibrous tissue is seen around the clip site.

Fig. 13 (Dog 55).—Photomicrograph of a silver clip anastomosis in the abdominal aorta, 165th postoperative day, with Weigert, Hematoxylin, and Van Gieson stains; × 20. The intimal surface faces downward. The intimal cleft is entirely bridged over and the intima is hyperplastic at this point. The media is joined by a transverse band of connective tissue. The blackened elastic tissue strands on the upper right represent the remnant of the everted edges. On the upper left, the granulomatous nature of the tissue in immediate contact with the silver clip is apparent.



three to four days, but complete reconstitution of the intima takes three to four months. Medial healing is seen in the completed stage as a thin fibrous band interrupting medial continuity. The everted edges are gradually absorbed, but a tail of elastic tissue still marks the site of anastomosis as late as five months postoperatively. Various stages in the healing process are seen in Figures 9 to 13.

In the area immediately surrounding the silver clips there is a layer of granulomatous tissue. Many of the macrophages seen in this tissue contain brown deposits, presumably of silver salt. The tissue surrounding the stainless steel clips is free of inflammatory cells.

COMMENT

In this research a method of anastomosis has been devised which appears to be more rapid than previous methods.

The double transections and reanastomoses done at the end of the series were accomplished in 8½ to 12 minutes. It is believed that any competent surgeon will be able to perform anastomoses by this method with equal rapidity.

This emphasis on speed in a period when surgery has been made safe for the patient, and gentleness and precision the major technical considerations, might well be questioned.

The virtues of speed become apparent in this special case when the time available for operation is considered.

The period of safe occlusion of the thoracic aorta in the dog has been determined by various observers to extend from 10 to 30 minutes.‡ Throughout this time interval, however, disasters may occur in the individual dog. In our own experience time beyond the 20th minute is extremely hazardous.

It is difficult to determine exactly for the dog the importance of such factors as age and size, but it was felt that younger and smaller animals, in general, withstood aortic occlusion best. Another undetermined factor is the effect of interrupting the intercostal

‡ References 6 through 12.

vessels. Spastic paralysis developed in our series after occlusion of 14 to 20 minutes. This inexplicable variation in the effect of occlusion is seen in the results of all investigations of the subject.

In the human, there is always an element of risk in aortic occlusion, regardless of the collateral circulation. Not only are the safe limits unknown, but the effects in the individual case are unpredictable. A more rapid method of anastomosis would appear to minimize this risk.

Until confidence in this method grows with clinical trial, it can be regarded as a rapid method of reestablishing blood flow. After release of occlusion clamps, interrupted sutures may be placed at leisure between the clips to reinforce the anastomosis.

Other investigators have devised methods to circumvent the danger of overlong occlusion.‡ These include internal or external shunts and local or general hypothermia. The effectiveness of these methods is shown indisputably by the experimental results. Local hypothermia is still uncertain enough in effect to warrant minimal occlusion, while generalized hypothermia has undesirable effects on the central nervous system and heart. The shunting procedures appear to be dependable but also have shortcomings. External shunts require additional arterial openings or sacrifice of vessels, while the internal shunts may be difficult to place and remove.

Other features of clip anastomoses that are demonstrated in this study are intima-to-intima approximation and absence of foreign material in the lumen. The sole case of thrombosis in the series followed faulty placement of a silver clip. The strength and stability of the clips is shown by the absence of postoperative hemorrhage.

Stainless steel would seem to represent the ideal material for clips as it combines strength and inertness within the tissues.[13]

A previous report of metallic suture of blood vessels was made in 1952 by the Hungarian investigators, Bikfalvi and Dubecz.[14] Their machine applies silver clips by means of a vessel-encircling mechanism, working on the principle of the von Petz clamp. The ingenuity of this method is intriguing although it possesses a number of serious disadvantages. Chief among these is its inflexibility. The apparatus presently in use can only be applied to vessels 6 to 8 mm. in diameter. In addition, the vessel wall must be of the correct thickness as the clips will fail to pass completely if it is too thick or it may crush the tissue between the compression rings. This inability to adjust tissue pressures is a serious failing of the method.

Although the placement of the clips is completely mechanized, the preliminary steps are time-consuming, and 14 to 18 minutes are required for a single anastomosis. Two references to previous reports of metallic suture cited in this paper were unobtainable.

There are numerous possible practical applications of the clips. In military and traumatic surgery they could be used in the anastomosis and repair of injured vessels. They seem to be ideally suited for surgical emergencies such as inadvertent incision of blood vessels, since they can be applied in confined spaces. They might also be used in closing arterial stumps too short for ligature. Rapid closure of incisions in the wall of the auricles or great vessels following valvular repairs might represent a use in cardiac surgery.

It is hoped that the clips may ultimately be produced in three sizes suitable respectively to arteries such as aorta, carotid and femoral, popliteal, and brachial.

A questionable aspect of clip anastomosis that deserves investigation is its behaviour in growing animals.

SUMMARY AND CONCLUSIONS

A method of blood vessel anastomosis by means of stainless steel clips is presented.

This method is felt to be more rapid than previous methods of anastomosis.

Results following the use of the clips are presented for arteriotomy wounds and single and double anastomosis of the aorta.

It is shown that the clips adhere to the requirments of a good vascular anastomosis.

Dr. Patrick J. Horan, Assistant Resident in Surgery at the Royal Victoria Hospital, aided in

the operative phase of research. Mr. Edward Taylor, Chief Machinist to the Department of Physiology at McGill University, was instrumental in the development of the arterial clip and the holding clamp used in this research.

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VINYON-N CLOTH TUBE FOR BRIDGING ARTERIAL DEFECTS

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DE BAKEY and Simeone,[1] Hufnagel,[2] Schloss and Shumacker,[3] and others have reviewed the development of techniques for restoring continuity of severed blood vessels by direct anastomosis and methods for bridging of arterial defects with the use of transplants of veins and arteries or tubes of glass, metal, or plastic. Transplantation of veins was recommended by Blakemore, Lord and Stefko, in 1942,[4] as an emergency method for bridging defects in severed primary arteries. This technique has been helpful for certain emergency problems. Vein grafts as tried experimentally for defects of the aorta by Shumacker, Schloss, Freeman, Wayson, and Stahl,[5] Nabatoff, Touroff, and Gross,[6] Sako and Varco,[7] Johnson, Kirby, and Hardy,[8] Schmitz and co-workers,[9] and others have usually dilated. Efforts to support vein grafts by Sako and Varco,[7] using pericardium, by Kanar and associates,[10] using dicetyl phosphate, and by others have not consistently prevented this complication. Bridging of arterial defects by the use of autografts has been successful experimentally, but few arteries of major size are available for this use in the patient. Hurwitt and Kantrowitz [11] report interesting experiments in which several short segments of splenic arteries were split longitudinally and then sutured side-to-side to form a tube of sufficient diameter for use in an aortic defect. Bridging of arterial defects using heterografts has been associated with many complications and failures. Use of arterial homografts has been more successful and preserved grafts were employed by Gross, Hurwitt, Bill, and Peirce,[12] 1948, as the first successful bridging of defects in the human aorta. Use of homografts, frozen or stored in solutions, is now a generally employed technique and has usually given satisfactory clinical results. However, experimental and clinical studies indicate that, unlike arterial autografts, these homografts degenerate and are almost entirely replaced by fibrous tissue. They, therefore, act as a satisfactory strut or prosthesis.

Carrel [13] used paraffined tubes of glass or aluminum experimentally, inserting these through longitudinal incisions in the thoracic aorta. Thrombosis occurred 12 days to 5 months after operation. Makins [14] quotes Tuffier as using silver tubes coated with paraffin for arterial injuries but thrombosis also occurred. Hufnagel,[2] 1947, used rigid tubes of methyl methcrylate across defects in the aorta of dogs and had no trouble with thrombosis, but hemorrhage occurred where ligatures attaching the aorta to the rigid wall of the tube cut through the aorta. In subsequent studies. Hufnagel,[15] solved this problem by use of nylon multiple-point fixation rings instead of ligatures; rigid plastic tubes containing a ball valve were successfully placed in the proximal aorta of patients with aortic insufficiency.

Semi-rigid polyethylene tubes were used to bridge defects in the thoracic aorta of dogs by Donovan.[16] Of nine animals, seven died after an average time of 51 days, embolism or rupture, and in two survivors the tube remained open at 6 and 8 months. Moore [17] placed polyethylene tubes across defects in

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Supported by a research grant from the Division of Research Grants and Fellowships of the National Institutes of Health, United States Public Health Service.

Presented at the meeting of the North American Chapter of the International Society of Angiology, San Francisco, June 19, 1954.

the thoracic aorta of rabbits and had difficulty with thrombosis; four animals survived 3½ to 10½ months. Neither author had serious trouble with hemorrhage from ligatures cutting through the aorta. Voorhees, Jaretzki, and Blakemore [18] first reported the use of pliable tubes made of Vinyon "N" cloth. The cloth was folded and stitched longitudinally to form tubes which were inserted into or sutured to either end of a defect in the aorta of dogs. Of 15 animals, 3 developed occlusion, and the remainder were open or only partially occluded up to the longest follow-up, 153 days. Hufnagel [19] currently reported use of a flexible plastic prosthesis, and Shumacker, Harris and Siderys [20] use pliable plastic tubes.

The present studies were undertaken in 1952 after a personal communication with Dr. Blakemore and his associates. The idea of testing a cloth tube seemed interesting, since such a tube avoids the difficulty of suturing the elastic aorta to a rigid prosthesis. Also the cloth can be tailored to any size or shape as an emergency need might develop. Assorted sizes and shapes of preserved homografts frequently are not available to surgeons. The porous cloth should permit ingrowth of fibrous tissue.

MATERIAL

The cloth, Vinyon-N *, is a plain weave fabric with 45 threads per inch. Each thread is a two-ply yarn, formed by twisting together two, 200-denier (gauge) yarns. The yarn is made from a resin, a copolymer containing about 60% vinyl chloride and 40% acrylonitrile. The cloth is sterilized by boiling; pressure steam autoclaving results in contraction of the fibers and hardening of the material. As used in these experiments a patch of single layer cloth, cut to appropriate rectangular shape and size, is folded and stitched longitudinally to form the tube.

PROCEDURE

Thirty mongrel dogs weighing 12 to 44 lb. (5.4 to 20 kg.) were used. They were anesthesized, with intravenous pentobarbital (Nembutal). Under sterile conditions the abdomen was entered through a left rectus incision. A segment of the aorta between the renal vessels and the bifurcation was mobilized and divided between serrated clamps. The ends of the vessel were allowed to retract; occasionally a small segment was excised. A tube of the Vinyon-N cloth, measuring 2 to 5 cm. in length was then used to bridge the defect. A continuous running everted suture of 0000 arterial silk moistened with mineral oil was employed to anastomose each end of the pliable tube to each end of the divided aorta. The distal clamp was released first. This allowed backflow of blood, some of which escapes through the fine mesh, filling the pores. The proximal clamp was then released. Brisk bleeding through the interstices of the cloth occurred for 10 to 40 seconds; all bleeding would then stop. Good pressure could be palpated in the prosthesis and good pulsations could be felt distal to the tube. The peritoneum was closed over the aorta and the prosthesis, and the abdomen was closed in layers. No anticoagulants were used and antibiotics were not give routinely. Patency of the cloth tube was determined by aortograms routinely made just before autopsy of killed animals, by autopsy of animals dying of complications, and by palpation of femoral pulses of animals now living.

RESULTS

Results of use of Vinyon-N cloth tubes are outlined in Table 1, 22 tubes with patent lumen and Table 2, 8 tubes with lumen occluded. Of the 30 dogs, 20 were examined at autopsy; 8 now living have palpable femoral pulses, and 2 dogs were lost. One of the missing dogs, No. 137, had an aortogram revealing patency at 60 days, the other, No. 142, had palpable femoral pulses when last examined at 30 days.

Of the 20 dogs examined at autopsy, the tube was patent in 12. A typical aortogram obtained just before autopsy is shown in Figure 1. The tube was occluded in eight; cause of obstruction varied. Infection around the prosthesis in one dog, No. 135, caused collapse of the tube but no deterioration of the fabric. Femoral pulses had disappeared on the 19th day. Cause of obstruction in two animals, No. 126 and No. 129, was partial disruption of the proximal anastomosis, the defect filled with an old thrombus which had propagated to include the lumen. Old thrombus was also found in four dogs in which

* Supplied through the courtesy of Dr. T. W. Nale, Union Carbide and Carbon Corp., New York, and Dr. W. Nelson Stoops, Carbide and Carbon Chemicals Co., South Charleston, W. Va.

the lumen of the tube evidently had not been adequate at the time of operation. Inadequacy was caused by a fold in the cloth in dogs No. 104 and No. 143, by use of a tube narrower than the aorta in dog No. 118 and by narrowing of the proximal anastomosis by misplaced sutures in dog No. 108. A fresh thrombus occluded the lumen of the tube at 30 days in another dog, No. 122, even though the suture line was intact and the lumen was not narrowed.

Of the 12 dogs with a patent prosthesis at the time of death, each had a smooth, glistening, pale or pink membrane lining the lumen of the Vinyon-N tube (Fig. 2). Dilatation was present in only one, slight sacculation of an area in the distal portion. This animal, No. 138, had been sacrificed on the 57th day. A small shallow thrombus was present in the middle of the prosthesis of dog No. 111, killed at 171 days (Fig. 3). This covered one-third of the diameter of the tube. A similar shallow thrombus was present in the distal portion of the prosthesis of dog No. 124, killed at 195 days. An irregularity of the lumen of a fourth dog consisted of a localized thickening of the glistening layer of fibrin. This projected 2 mm. into

TABLE 1.—*Vinyon-N Tube, Aorta Patent*

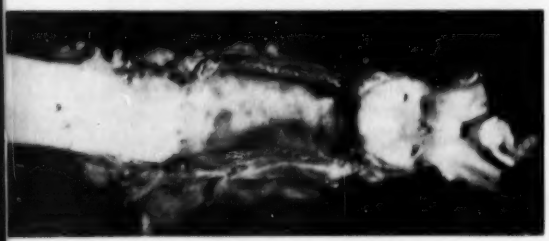
Dog, No.	Weight, Lb.	Aorta Clamped, Minutes	Survival, Days	Remarks
1. 111	23	35	171	Isolated thrombus in lumen of tube
2. 115	18	30	5	Death due to abdominal evisceration
3. 117	16	37	250	.....
4. 119	20	42	241	.....
5. 120	19	40	38	Excess fibrin in proximal part of tube
6. 121	15	22	240	.....
7. 123	44	49	86	Hind limb paralysis
8. 124	25	22	195	Isolated thrombus in lumen of tube
9. 125	12	22	Alive	Aortogram reveals patency
10. 132	18	50	Alive	Palpable femoral pulses
11. 133	21	70	3	Died of aspiration pneumonia
12. 134	24	24	10	Died of septicemia from pre-existing osteomyelitis
13. 137	33	35	Missing	Aortogram revealed patency at 60 days
14. 138	23	35	57	Died night of aortography
15. 139	21	42	Alive	Palpable femoral pulses
16. 140	26	32	70	.....
17. 141	18	32	Alive	Palpable femoral pulses
18. 142	25	42	Missing	Pulses palpable at 30 days
19. 144	15	35	Alive	Palpable femoral pulses
20. 145	23	60	Alive	Palpable femoral pulses
21. 146	25	30	Alive	Palpable femoral pulses
22. 147	25	30	Alive	Palpable femoral pulses

TABLE 2.—*Vinyon-N Tube and Aorta Occluded*

Dog, No.	Weight, Lb.	Aorta Clamped, Minutes	Survival, Days	Remarks
1. 135	20	35	22	Infection about tube
2. 126	33	30	166	Proximal anastomosis disrupted
3. 129	15	27	149	Proximal anastomosis disrupted
4. 122	23	27	36	Thrombosis at 30 days
5. 108	19	25	360	Proximal anastomosis partially sutured together
6. 118	17	40	40	Prosthesis smaller than aorta in diameter
7. 104	17	34	222	Obstruction where kinking of tube occurred
8. 143	15	22	57	Fold in center of tube producing obstruction

Fig. 1.—Aortogram showing the lumen of a Vinyon-N tube bridging a 4-cm. defect in the mid-abdominal aorta of a dog and the uniform diameter of the abdominal aorta proximal and distal to this tube. Aortogram was obtained 171 days after the cloth tube was sutured into the defect.

Fig. 2.—Specimen removed from a dog killed 250 days after insertion of a Vinyon-N cloth tub. The aorta and tube have a uniform diameter. The fibrous tissue about the cloth is collagenous and relatively acellular. The intima lining the tube shows moderate patchy proliferation.



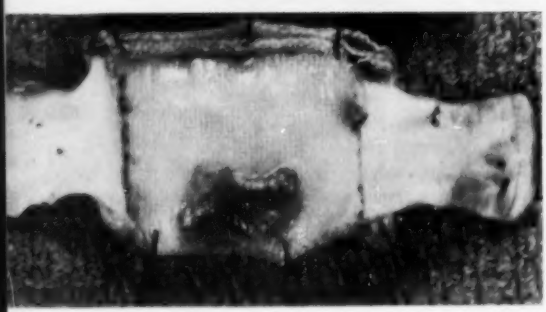
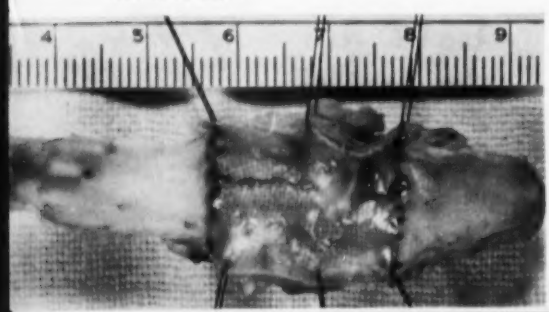


Fig. 3.—Small shallow thrombus present under the endothelium of a Vinyon-N cloth tube at 171 days.

Fig. 4.—Excess deposit of fibrin located under the endothelium and partialy puckering the cloth tube at 38 days.



the proximal portion of the prosthesis (Fig. 4). Only 1 (No. 132) of the 12 dogs with patent lumen which were killed had developed partial paralysis of hind limbs. Microscopic examination of the spinal cord revealed myelomalacia.

The remaining eight animals are still living and have palpable femoral pulses in each leg.

HISTOLOGIC STUDIES

The aortas and the Vinyon-N tubes were removed during autopsy and fixed for one week or more in 10% formalin. Cross and longitudinal sections were taken of each specimen. Since the fabric would not cut readily after routine preparation, it was necessary to dissolve and remove part of the Vinyon-N before embedding in paraffin. Therefore, after blocks of formalin-fixed tissue had been dehydrated in alcohols, they were transferred to acetone. During 8 to 12 hours and several changes of acetone, the synthetic fibers became soft enough for cutting. The blocks were then transferred in succession to chloroform, chloroform-paraffin, and paraffin and then easily cut. Sections were stained with hematoxylin and eosin, Verhoeff-Van Gieson procedure, Masson stain or, occasionally, with Wilder reticulum stain or the Holmes' stain for nerve fibers.

Microscopic examination revealed that the specimens of animals sacrificed at three and five days were covered on both surfaces and in the interstices of the cloth by a fibrinous exudate in which polymorphonuclear leukocytes, lymphocytes, and plasma cells were present in moderate numbers. There was comparatively more exudate on the external surface than on the internal surface. A small pocket of similar fibrinous material filled the triangular space between the everted edges of the aorta and the cloth (Fig. 5*A*). The everted free portion of the edges of the aortas were necrotic. One specimen was examined at 10 days. Partial organization of the external fibrinous layer was present, but there was no organization of the inner layer at this time.

Another specimen was examined at 22 days. The external fibrinous layer was almost completely organized, whereas this process was incomplete in the inner fibrinous layer. Organization of the inner layer had proceeded by growth of fibroblasts from the terminal edges of the aorta and through the interstices of the cloth from the outer organized layer. The inflammatory infiltrate of both layers was considerably decreased in amount as compared with the 10-day specimen, although foreign body reaction with multinucleated cells was now present in and about the cloth and about the suture material.

In three specimens obtained between 36 and 40 days the inner layer was organized and covered by a thin layer of endothelium arising from the aortic endothelium at the junction of the aorta and the cloth (Fig. 5*B*). On the inner surface of the aorta adjacent to the proximal orifice of the tube a small nodule of thickened endothelium was occasionally observed. On the inner surface of the tube, occasionally, there were small hemorrhages. Lymphocytes and plasma cells had largely disappeared, but the foreign body reaction persisted about the cloth and the sutures. One tube examined at 86 days showed evidence of continued organization. The lumen of the tube was completely lined with typical endothelium continuous with the aortic endothelium.

Tubes from nine dogs killed between 149 and 300 days demonstrated further organization of the cellular fibrous tissue into a more collagenous, relatively less cellular tissue. The intima of the aorta proximal to the tube frequently showed a moderate degree of proliferation; the adjacent intima of the tube had similar changes (Fig. 5*C*).

There was no evidence of development of neoplasm in any of the tissues examined. The fibroblastic cells in the organizing tissue showed no more atypical processes than those present in ordinary wounds. Typical endothelium covered the lumen of each of these tubes. When recent thrombi were noted the endothelium was present beneath them. Old thrombi were covered by endothelium.

CONCLUSIONS

Pliable cloth tubes of Vinyon-N fabric have proved convenient and usually satisfactory as prostheses for bridging defects in the abdominal aorta of dogs. Fibrinous exudates early permeate and surround the tubes, and later organize into a more col-

Fig. 5.—Junction of proximal aorta and Vinyon-N cloth at 5 days (*A*), at 39 days (*B*), and at 240 days (*C*), showing progressive organization of the fibrinous exudate (*A*), growth of endothelium from the aorta (*B*), and complete endothelium covering a relatively acellular and collagenous fibrous tissue union and support (*C*). The Vinyon-N fabric was dissolved before cutting these sections.

lagenous and relatively less cellular tissue which maintains good support. Endothelium proliferates over the lumen from the adjacent aorta. The lumen remained patent in 22 of 30 dogs and slight dilatation was present in the distal portion of but one tube. Sutures between aorta and cloth separated infrequently and massive hemorrhage did not occur. Nevertheless, there is as yet insufficient evidence of late results to warrant use of cloth tubes in place of arterial homografts in man unless these are not available.

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CRITERIA FOR AND RESULTS OF TRANSMETATARSAL AMPUTATION FOR ISCHEMIC GANGRENE

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THE MANAGEMENT of gangrene and infection of the lower extremities associated with arteriosclerosis and diabetes has made important strides since the advent of antibiotics. With the control of most foot infections, a more conservative treatment of the necrotic lesions per se has become possible. Whereas before the use of antibiotics major amputations were frequently unavoidable, since their availability local foot surgery, in selected cases, has become feasible and safe and has often resulted in salvage of the limb.

TABLE 1.—*Major Amputations Performed for Ischemic Gangrene from 1949 through 1953*

	Number	Percentage
Midleg	118	61
Transmetatarsal	59	30
Midthigh	18	9

Good results following transmetatarsal amputation for ischemic gangrene and infection in 75 patients with diabetes were first reported by McKittrick in 1946.[1] Subsequently, Furste and Herrmann in 1948,[2] McKittrick and his associates in 1949,[3] Warren and his associates in 1952,[4] and others * further emphasized the value of this conservative surgical procedure.

With the introduction of the transmetatarsal amputation into the surgical armamentarium, there was good reason to believe that the incidence of major amputations could be reduced. Our experience at Montefiore Hospital lends support to this belief. During the period extending from 1949 through 1953, transmetatarsal amputation represented 30% of the total major amputations (Table 1). It is the purpose of this paper to discuss in the light of this experience the criteria for the selection and the results of transmetatarsal amputation in patients with gangrene, ulceration, and infection of the toes, associated with obliterative arterial disease. This study is based on an experience with 59 cases.

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Presented at the meeting of the North American Chapter of The International Society of Angiology, San Francisco, June 19, 1954.

* References 5 and 6.

CRITERIA

It is important to point out that many of the patients of this series had received medical treatment for long periods, ranging from six weeks to several months, prior to the surgical procedure. After failure of the medical treatment, indication for a transmetatarsal amputation was arrived at after evaluation of local factors which are discussed in this paper.

Gangrene.—The main indication for a transmetatarsal amputation is gangrene of one or more toes (Fig. 1). A sharp line demarcating the lesions is a favorable sign for the successful outcome of the procedure. In contrast, absence of a line of demarcation, usually indicating a spreading process, should be considered as a contraindication to the procedure. In cases of recent gangrene, it is important to wait for the development of a sharp line of demarcation before the level of amputation can be safely decided upon. In some selected cases, involving the first or fifth toe, single toe amputation may be carried out with reasonable chance of success. However, my experience indicates that it is always safer to perform a transmetatarsal amputation, especially when more than one toe is involved.

Chronic Ulceration.—Chronic ulceration of toes or of the ball of the foot frequently

develops in patients with occlusive arterial disease and diabetes. These lesions usually involve the plantar surface under a meta-

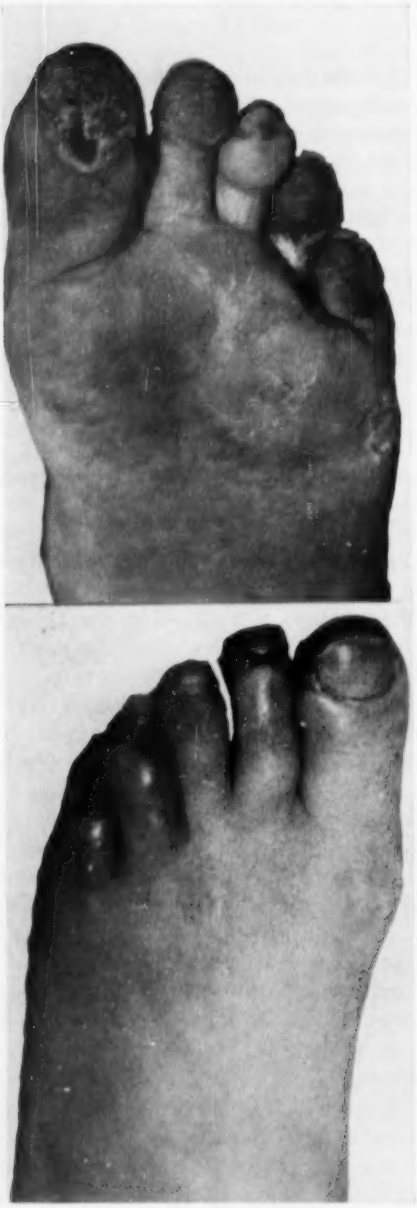

Fig. 1.—Gangrenous lesions involving all the toes in a nondiabetic, arteriosclerotic patient with absent femoral pulse. Note plantar callus at the level of the fifth metatarsal head. His stump healed by delayed union.

Fig. 2.—Illustration showing dorsal, plantar, and medial views of the lines of skin incision for transmetatarsal amputation.

tarsal head and appear as an open infected area surrounded by thick callus leading to a denuded tendon or joint. While such lesions often heal on bed rest and local dressings, the associated diabetic neuropathic condition and the occasional underlying osteomyelitis of the metatarsal heads appear to be responsi-

Fig. 3.—Illustration showing (*a*) the short dorsal and long plantar flaps, and (*b*) the stump after approximation of the flaps.

ble for their great tendency to recur. In these cases, transmetatarsal amputation performed "through skin with normal sensation" as noted by McKittrick and associates [3] is of value.

Local Infection.—Local infection frequently associated with the gangrenous or ulcerative lesions can usually be controlled either by antibiotics alone or in combination with adequate drainage. After the infection has been brought under control, a closed amputation can be performed safely. However, in cases with uncontrollable infection due to invasive deep suppuration, it was found both more expedient and safer to perform an open amputation. In 10 of the 59 cases (17%), this procedure was necessary and proved valuable.

Condition of Areas Adjacent to Lesions.—Evaluation of the status of the tissues proximal to the involved toes is essential in determining the advisability of a transmetatarsal amputation. Permanent cyanosis and shiny thin skin with marked loss of subcutaneous tissue indicate advanced ischemia of this area and contraindicate the procedure. In contrast, local edema due to dependency and osteomyelitis of the metatarsal bones do not preclude a successful outcome. It is essential that dependency edema be eliminated by the horizontal position of the lower extremity before the operation. The presence of osteomyelitis, despite the use of antibiotics, may necessitate an open procedure.

Circulatory Status.—In attempting to evaluate the degree of arterial insufficiency, clinical criteria usually provide most of the desired information. While the presence of a popliteal or pedal pulse appears to insure prompter healing of the amputation wound, absence of these pulses does not represent a contraindication to surgery at this level. Thus of 44 successful cases in whom the wound healed either by primary or secondary intention, 2 had an absent common femoral pulse, 24 had an absent popliteal pulse, and only 18, or 41%, had a palpable popliteal artery. Of the latter, 6, or 13%, had also one palpable pedal artery. In the 13 unsuccessful cases, the popliteal pulse was felt in 3 or in 23% of the cases. From these findings it appears that while a patent popliteal artery may be a favorable factor, nevertheless it does not represent an absolute criterion in the selection of the transmetatarsal level for amputation. In contrast, the degree of collateral circulation available in the forefoot appears to be the decisive criterion. Postural color changes and skin temperatures at various levels of the foot, determined under basal conditions, may be helpful in evaluating the degree of collateral circulation. Rapid blanching of the forefoot on elevation and the presence of a sharp difference in skin temperature between the midfoot and the forefoot indicate poor arterial supply to the latter. In my series, these signs have been associated with failure of the procedure.

Local Pain.—Local pain usually associated with gangrene or infected ulcerative lesions is not a contraindication to this procedure. However, radiating pain toward the ankle or leg, often unrelieved by narcotics, indicates poor prognosis and should be regarded as a contraindication to transmetatarsal amputation.

Finally, in assessing the local factors, it is also important to consider the initiating cause of the lesions, their duration, the status of the other lower extremity, and the general condition of the patient.

TECHNIQUE

In addition to the use of adequate antibiotics for the control of the infection always present in these foot lesions, great emphasis is attached to preoperative asepsis of the skin. With McKittrick and associates [3] and Smithwick,† I feel that the successful outcome of the transmetatarsal amputation is greatly enhanced by local preparation of the operative field. This is particularly important when a closed amputation is contemplated. Careful washing of the foot with pHisoderm or surgical soap (Septisol) and water once or twice daily for a period of about a week was used in all our cases.

The actual technique of amputation was essentially that described by McKittrick and associates,[3] except for a few details which will be mentioned. The lines of the skin incision are shown in Figures

† Smithwick, R. H., in discussion of the paper by McKittrick and others,[3] p. 841.

2 and 3. The dorsal line is at the midshaft level, while the plantar is at the level of the metatarsal heads. The toes are disarticulated, and the metatarsal bones with their respective tendons are separated from the plantar flap through the cleavage spaces, thereby avoiding any unnecessary trauma. Each bone is divided at the midshaft level, using a Gigli or a Strycker saw, and, in some cases, if necessary, further shortened with a rongeur. The tendons are excised and any loose tissue is carefully trimmed away. The wound is washed with warm saline and hemostasis is carefully secured. No forceps are used in handling the flaps. It cannot be overemphasized that atraumatic handling of these ischemic tissues is essential since the margin between success and failure may be very slight.

In a closed transmetatarsal procedure the flaps are approximated without tension, using fine nonabsorbable (surgical) silk, and without drainage. In an open transmetatarsal procedure the wound is loosely packed with plain gauze and a continuous wet dressing is instituted.

Postoperative Care.—The foot is placed on a foam rubber pillow, in a slightly dependent position. A cradle is placed over it to protect the stump from any trauma. Administration of antibiotics is continued for about three weeks or longer if necessary.

In an open transmetatarsal amputation, the wet dressing is continued for one to three weeks until the local infection clears up. The dressing is changed daily and the wound is irrigated with an antibiotic solution.

In a closed amputation, half of the sutures are removed after 10 to 14 days and the remaining sutures a few days later.

After healing of the stump, resumption of weight-bearing is delayed by about two weeks. The patient is then instructed to use properly fitted shoes, cautious ambulation, and a continuous program of foot care.

RESULTS

During the five-year period extending from 1949 through 1953, a total of 59 transmetatarsal amputations were performed in 56 patients (3 patients had a bilateral amputation).‡ Of these patients, 48 had arteriosclerosis obliterans and diabetes; 7 had arteriosclerosis without diabetes, and 1 had thromboangiitis obliterans. There were 41 men and 15 women. The age of the patients varied as follows: in the diabetic male group the age distribution ranged from 51 to 78, with an average of 65; in the diabetic female group, from 55 to 82, with an average of 57; in the nondiabetic group (all but one were males), from 62 to 82, with an average of 69.

Immediate Results.—Closed Amputation: The immediate results of transmetatarsal stump healing after primary closure are shown in Table 2. From this table it appears that 39.1% of the cases healed by primary union, and 34.8% healed by delayed union, and 26.1% required a reamputation at a higher level. Healing by primary union usually occurred within three to four weeks (Figs. 4 and 5). Delayed union usually was due to marginal necrosis of either the dorsal or plantar flaps, requiring about 4 to 6 months for the wound to heal.

Table 2.—*Results of Transmetatarsal Stump Healing after Primary Closure in Patients with Arteriosclerosis*

	Cases, No.	Primary Union	Delayed Union	Reamputation
Diabetic	38	15 (39.5%)	12 (31.6%)	11 (28.9%)
Nondiabetic	8	3 (37.5%)	4 (50%)	1 (12.5%)
Total	46	18 (39.1%)	16 (34.8%)	12 (26.1%)

Open Amputation: Of the 10 cases of open transmetatarsal amputation 9 healed and 1 failed. In all these cases the gangrenous lesions were associated with invasive uncontrollable infection, the latter representing the chief indication for the open procedure (Figs. 6 and 7). Healing of the stump occurred within three to four months.

Hospital Mortality.—Three patients of the 56, or 5.3%, died after the operation. Two deaths were due to acute myocardial infarction and occurred 24 and 72 hours postoperatively. The third death was due to amyloidosis and occurred five months postoperatively, the stump showing delayed healing due to marginal necrosis. Five other patients of this series died while in the hospital from

‡ While most of these amputations have been performed by me or done under my supervision, several members of the attending and resident staffs on the P. V. D. Service have also performed a certain number of them.

Fig. 4.—Gangrenous foot lesions involving the first, second, and third toes treated successfully with transmetatarsal amputation.

Fig. 5.—Result of stump healing after primary closure.

Fig. 6.—Gangrene of the third toe and of the adjacent two toes (the lesion of the fourth toe not visible on the photograph). Note blister and underlying necrotic lesion of the dorsum at the level of the third toe. These lesions were associated with deep invasive infection uncontrollable by antibiotics. An open transmetatarsal procedure was performed.

Fig. 7.—Result of stump healing of the open transmetatarsal amputation three and one-half months later performed for lesions shown in Figure 6.

an intercurrent disease or another surgical procedure not directly related to the transmetatarsal amputation.

Follow-Up Results.—The follow-up study ranges from a minimum of 5 months to a maximum of 51 months, with an average of 25.5 months. Of 41 patients healed at the time of discharge or shortly thereafter, 4 developed gangrene (2 on the stump and 2 on the heel), requiring a subsequent midleg amputation. Time elapsed between the transmetatarsal and midleg amputation ranged from 18 to 46 months. The late gangrene resulted from spontaneous breakdown of the stump in 1, accidental burn of the stump in 1, and pressure of the heel in 2. Four other patients developed ulcers of the plantar surface of the stump, mostly at the level of the first metatarsal bone. The ulcer appeared in the center of a thick callus and seemed related to weight-bearing. In addition to the latter factor, diabetic neuropathy and ischemia of the tissues were also present and probably contributed to the breakdown of these vulnerable areas of the stump. While the majority of these patients need no special shoe, those with recurrent ulcers require the use of a tarsal bar. By shifting the weight-bearing center away from the metatarsal ends, recurrence of such ulcers is eliminated usually within a few weeks. The over-all functional results were good to excellent. The patients walk without a limp and usually without a cane.

The patients who developed late gangrene or ulcerations of their stump had a useful foot until the time of their complication. Eight patients of this follow-up group died at intervals of 6 to 25 months after hospital discharge of causes unrelated to the transmetatarsal amputation.

COMMENT

The indications for transmetatarsal amputation are based primarily upon evaluation of local factors. In patients with marked arterial insufficiency it may be difficult sometimes to forecast the outcome of this amputation. With experience, however, in most cases the indications can be arrived at by adhering to the evaluation of local factors. Similar criteria are valuable guides in the choice of the other levels of amputation for ischemic gangrene of the lower extremities. Such criteria have recently been reviewed in the light of an experience of the P. V. D. Service based upon 455 major amputations performed from 1939 to 1954.[7]

Transmetatarsal amputation for ischemic gangrene can be credited with reduction in the incidence of higher amputations. Proper indication and careful surgical technique are essential if a high percentage of success is to be achieved. From the preceding data it appears that the success of a transmetatarsal amputation for ischemic gangrene of the toes, ulceration, and infection depends upon several factors, the most important being (1) well-demarcated lesions, (2) well-controlled infection, (3) adequate collateral circulation at the amputation level, (4) selection of proper time for operation, (5) careful and adequate preoperative asepsis of the skin, and (6) careful atraumatic technique.

McKittrick and associates,[3] in their series of 215 cases, reported 155 (72%) healed at the time of their hospital discharge. Later, follow-up indicated that 67% of the entire group had satisfactory results. Warren and associates,[4] reporting on 43 cases, showed an incidence of 62.8% successful healing. Likewise, late results of these cases showed that the majority of the patients had a useful foot and that only 3.7% required higher amputation.

In the present series, healing occurred in 73.9% of the cases with the closed procedure and in 90% of the cases in the open procedure. Over-all healing occurred in 77% of the cases. The difference in the percentage of the successful results between the two groups is a reflection of a better arterial supply in the latter cases rather than of other factors. In this connection, it is of interest to note that all the patients in this series had foot lesions associated primarily with arterial insufficiency. Similar lesions due to infection, osteomyelitis, and neurogenic disturbances in the presence of good arterial circulation should be distinguished from those due to

ischemia of the tissues. In the former cases a transmetatarsal amputation usually results in prompt healing. Thus McKittrick and associates [3] in 70 cases had only 1 failure, and Warren and associates [4] reported 8 cases, with no failure. It is therefore important for a correct interpretation of the results of transmetatarsal amputation to make a clear distinction between these two types of foot lesions.

Analysis of the clinical findings in the 13 cases of this series resulting in failure indicates that, notwithstanding apparent demarcation of the lesions, marked blanching of the forefoot on elevation and sharp difference in skin temperature between the forefoot and midfoot were present in 10 cases. In addition, severe rest pain, unrelieved by narcotics, was present in all these patients. While in the face of such signs of advanced ischemia of the tissues at the metatarsal level one might have an occasional success, these signs should be regarded nevertheless, as contraindication to the procedure.

The over-all results obtained in this series are gratifying and recommend transmetatarsal amputation as a limb-salvaging procedure. A follow-up study showed that 74% of the patients had satisfactory results. Although the hospital stay of many of these patients was relatively long, their complete rehabilitation fully justified the efforts surrounding their treatment. The advantages of this procedure cannot be overemphasized, especially in this old-age group of patients, in whom a higher amputation usually results in permanent invalidism.

SUMMARY

Criteria for the selection of patients with gangrene and infection associated with obliterative arterial disease with or without diabetes for transmetatarsal amputation are discussed. Emphasis is placed on careful evaluation of local factors as a guide to this selection.

Fifty-nine transmetatarsal amputations were performed in 56 patients, with a postoperative mortality of 5.3%.

Stump healing after primary closure occurred in 73.9% and after open procedure in 90% of the cases. Over-all healing occurred in 77% of the cases.

A follow-up study of 41 cases showed that 37 had good functional results, and 4 had late gangrene requiring a midleg amputation.

Factors favoring successful transmetatarsal amputation are the following: (*a*) well-demarcated lesions of one or more toes; (*b*) well-controlled infection; (*c*) adequate collateral circulation at amputation level; (*d*) selection of proper time for operation; (*e*) careful and adequate preoperative asepsis of the skin and (*f*) careful atraumatic surgical technique.

Unfavorable factors to a successful amputation are the following: (*a*) marked blanching of the forefoot on elevation; (*b*) sharp difference in skin temperature between the forefoot and the midfoot, and (*c*) persisting severe rest pain.

Excellent rehabilitation of the patient is the great advantage of the transmetatarsal amputation, since it allows walking without prosthesis.

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CONSIDERATION OF TECHNIQUE OF AORTIC EMBOLECTOMY

Presentation of Six Cases

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THE PROMISING results in valvular surgery have radically altered the outlook in rheumatic heart disease. As one consequence, the attitude toward arterial embolism, a characteristic complication, has also changed. This condition need no longer be considered an accelerated step in the downhill course of the hopeless invalid. It is, rather, an unfortunate episode which may be handled successfully in a patient who does have a chance of benefiting from subsequent cardiac surgery. In a review of more than 500 cases of mitral commissurotomy with a preoperative embolism incidence of 18.9%, Glover has observed only one questionable occurrence of cerebral embolism during a mean postoperative period of more than three years.*

The most dramatic and dangerous of all types of arterial embolism is that of lodgment at the bifurcation of the aorta. Whether the embolus remains there or slips down into the iliac vessels, the mortality is high and gangrene of the inferior extremities common. It probably comprises about 5% of embolism at all arterial sites, although there is good reason to believe that it is more frequent than a review of the literature would indicate.

The survey of Albright and Leonard, in 1950, listed 193 patients, of whom 144 died, 19 survived with loss of limb, and 26 were successfully treated by embolectomy.[1] It should be noted that the average survival time of these fortunate ones was 22 months, the mean being considerably less. Since that report, the proportion of reported successes is considerably higher, although the total comes to only about 40.† Of these, two have had subsequent mitral commissurotomy.

In the literature, the term "successful" has various shades of meaning. It is used to designate cases with restoration of pulses regardless of survival time; cases with viable, pulseless extremities, and cases surviving with minimal tissue loss or paralyses.

The factor essential to success is promptness of intervention. However, in the absence of obvious tissue death, operation should not be denied within 24 hours. In one of the cases herein described, an extremity survived although blood flow was not reestablished until 26 hours after embolism. In fact, there are two recorded cases of extremity survival in which embolectomy was performed 32 and 33 hours after occlusion.‡

The operative attack can be one either of direct aortotomy or of indirect removal of the embolus through iliac or femoral arteriotomies. The former method was employed in the first successful removal of an aortic embolus by Bauer, in 1913.[9] He entered the abdomen through a lower midline incision, packed off the small bowel, and evacuated the embolus through a linear incision in the aorta which was compressed above by an assistant's fingers. Madden has recently emphasized the desirability of this maneuver as a way of avoiding the use of clamps.[10] A variation of this direct approach was described by Linton, who incised the right common iliac artery and milked the clot out while occluding the aorta and iliac vessels with modified Bethune tourniquets.[11] Murray

From the Surgical Service of the Mount Sinai Hospital.

Presented at the meeting of the North American Chapter of The International Society of Angiology, San Francisco, June 19, 1954.

* Glover, R. P.: Personal communication to the author.

† References 2 through 6

‡ References 7 and 8.

used a retroperitoneal abdominal approach and also incised the right common iliac artery.[7]

When the condition of the patient is poor, an indirect approach has been employed. Credit for the first use of catheters, suction, and irrigation in the dislodgment of emboli must go to Handley, who, in 1907, failed to clear completely an iliac embolus with propagated clot, despite a valiant effort.[12] In his desire to do a complete arterial toilet, he opened the popliteal artery and passed fine catheters through in an attempt to clear the channel well down the extremity. The disadvantage of the indirect method is illustrated in two of the cases described below. It is not always possible to remove all embolic material in this manner. Furthermore, in the presence of arteriosclerosis, a site of arteriotomy may itself develop into a technical problem owing to splitting of the vessel wall and stripping of the endothelium. Other factors not usually considered but of importance in our group of cases are the relative length and caliber of the common iliac arteries, the level of bifurcation of the aorta, and the presence of duodenal overhang or a horseshoe kidney.

When feasible, the more satisfactory method is to first expose both femoral arteries. This allows confirmation of the diagnosis and, in the event of sudden deterioration, permits indirect embolectomy. Serrefines are applied to each femoral artery. The abdomen is then opened, the aorta exposed, and a catheter passed about it. Aortotomy is performed in the concavity of the bifurcation (Fig. 7). This allows easier evacuation of clot and subsequent suture. After closure of the abdomen, the femoral arteries are inspected for debris by performing transverse arteriotomy. Distal arterial irrigation and clearing are done through these openings. With completion of the procedure, the extremities are carefully examined. If there is any doubt of arterial clearance, further arteriotomy, usually popliteal, is carried out.

Although spinal anesthesia has its advantages, it is too hazardous in this type of case. Either general or a combination of general and local anesthesia is preferable.

Systemic anticoagulants are to be avoided. In two of our cases hemorrhage followed their use. The employment of drugs and sympathetic blocks is distinctly ancillary. If the plumbing job is well done, they are unnecessary.

REPORT OF CASES

CASE 1 (Fig. 1).—S. D., Hosp. 634723, a 58-year-old clerk, had been a known rheumatic for 25 years and had been on digitalis for 3 years. Four hours before admission, on Dec. 15, 1951, he experienced sudden numbness of both inferior extremities and inability to move them. Physical examination revealed a middle-aged man in fair general condition. His pulse rate was grossly irregular at 64; there were systolic and diastolic murmurs at the apex, and the heart seemed enlarged to the left. There were scattered rales at both bases. There were neither pulsations nor oscillations to be obtained, and not even an aortic pulse could be felt. With the patient under general anesthesia, the right femoral artery was first exposed and found empty. Laparotomy was then performed. Exploration revealed a high bifurcation of the aorta behind a large horseshoe kidney, with two long common iliac arteries coursing over the vertebral column. As they were being exposed, they suddenly started pulsating. Inspection showed the right femoral artery pulsating and, on exposure, the left as well. The wounds were closed, and the extremities were carefully examined. There were oscillations in the left thigh and leg, but the right leg remained cold below the knee and pulseless. Accordingly, right popliteal arteriotomy was done, and an embolus was removed from a point 4 in. (10 cm.) above the incision. After closure, the vessel was left pulsating. Through an accident the patient was given 300 mg. of depot heparin immediately, and four hours later, another 200 mg. Ten hours thereafter, the clotting time was 46 minutes. Three units of blood and 150 mg. of protamine sulfate were administered.

However, the patient went into shock, and 300 cc. of blood was released from the thigh wounds and another 200 cc. from the abdominal incision. His condition gradually improved. Both feet were warm and of good color, with normal sensation. All pulses were palpable except the right dorsalis pedis. On the fifth postoperative day there was some dark drainage from the abdominal wound. Inspection revealed a loop of small bowel with a small perforation in it. The hole in the intestine was closed, and the wound was secondarily sutured with wire. The patient did well and was allowed up, when, on the seventh day, he suddenly died. Autopsy revealed chronic mitral and aortic valvulitis, with

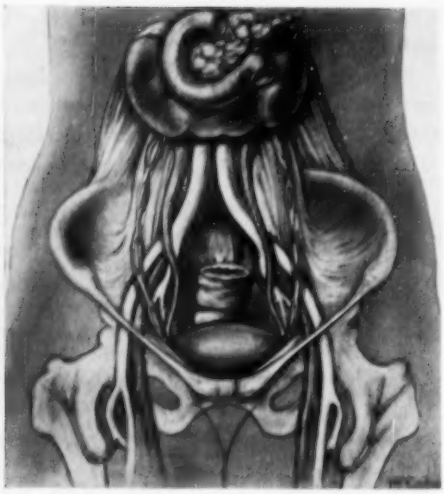


Fig. 1 (Case 1).—Note the large horseshoe kidney lying anterior to the high bifurcation of the aorta. The common iliac arteries are long and lie in parallel fashion on the vertebral column.

hypertrophy of the right ventricle and left atrium, multiple small pulmonary emboli, atherosclerosis of the aorta, a horseshoe kidney, and thrombosis of the left iliac vein.

Comment.—The actual cause of death was not established by autopsy. It probably was ventricular fibrillation. The lumen of the aorta at its bifurcation appeared constricted between the large kidney and the third vertebra. It was clear how the embolus removed from the lower femoral artery could occlude the bifurcation, which was also unusual in that the mouths of the iliac arteries faced cephalad instead of obliquely, as is usual. The importance of spasm in the mechanics of embolic occlusion has been stressed by Atlas.[18] Unfortunate accidents with postoperative anticoagulants do occur. If major arteries are well cleared of emboli and clot, the risk is certainly greater than the advantage.

Case 2 (Fig. 2).—S. R., Hosp. 624889, a 38-year-old housewife, had suffered from rheumatic heart disease for 10 years. Dyspnea on exertion had been present for 30 months, and only 7 weeks previously there had occurred transient coma, with tinnitus. Four hours before admission, on April 12, 1951, her feet had suddenly become numb and she was unable to stand because her "legs were paralysed."

Physical examination showed a young-looking woman in fair condition, with an irregular pulse, an enlarged heart, and systolic and diastolic murmurs at the apex. The lungs were clear, and the liver edge was down only 1 fingerbreadth. Both inferior extremities were cold, with absent pulses, no oscillations, and loss of epicritic sensation from midleg down. With the patient under spinal anesthesia, two teams exposed both femoral arteries. Since a transmitted pulsation was palpable at the inguinal ligaments, arteriotomies were placed inferior to the profunda femoris branches and the emboli were extracted from below. After the flow was established, the distal arterial tree was cleared on both sides. After operation, both feet became warm and of good color; the left foot pulses were immediately palpable, but it was not until the 10th postoperative day that the right foot pulses were constantly felt. The patient was out of bed on the 11th day and was transferred to the medical department for further investigation, where, on the 17th day, she suddenly died. Autopsy revealed chronic rheumatic heart disease, thrombosis of the right femoral vein with pulmonary infarction, and the presence of a thrombus at the right femoral arteriotomy site. The cause of death was given as probably cerebral embolism.

Comment.—This embolus had quite evidently split down the iliacs. The plan of operation was obvious. Although it is possible that a clot did form along the suture line in the right femoral artery, it is at least as likely that embolic material came down from above after arteriorraphy. It is not

Fig. 2 (Case 2).—Note that there is considerably more embolic material on one side.

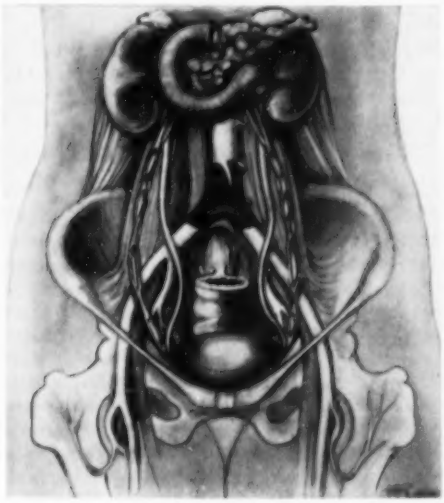


Fig. 3 (Case 3).—Note the location of the incision in the aorta. The vessel bulged with the large amount of embolic material packed in it.

uncommon to obtain more clot after it appears that the full arterial flow has been restored. For this reason, it is unwise to assume that a diminished pulsation in an artery is due to spasm unless there is clear-cut response to warmth and procaine hydrochloride (Novocaine). A short transverse arteriotomy is preferable to speculation. This is the chief disadvantage of probing for emboli.

Case 3 (Fig. 3).—L. H., a 56-year-old housewife, was admitted to Doctors Hospital on Oct. 29, 1951. She suffered from chronic cardiac valvular disease, mitral stenosis, and auricular fibrillation. That day there occurred a sudden onset of left hemiplegia, without loss of consciousness. On Nov. 5, 1951, she experienced acute abdominal pain which radiated into both inferior extremities. Physical examination revealed a restless aphasic pale sweating middle-aged woman, with cold, insensate, and pulseless inferior extremities. She had already been given 200 mg. of bishydroxycoumarin (Dicumerol) and 200 mg. of depot heparin. Because of her desperate condition, the left femoral artery was opened five hours later, with the use of local anesthesia, and an unsuccessful attempt was made to clear the obstruction from below. General anesthesia was then started, and the aorta was exposed through a lower midline incision. An easily palpable, solidly packed mass filled the terminal 2 in. (5 cm.) of the aorta, extending for ½ in. (1.2 cm.) into each iliac artery. With catheter occlusion of the aorta, it was possible easily to evacuate the clot through a ¾-in. (1.9 cm.) incision along the concavity of the bifurcation. It was closed with a running 00000 suture. Both feet became warm and of better color, and the right dorsalis pedis pulse was palpable. One hour after return to her room, it was noticed that the dressings were blood-soaked. She was returned to the operating room, where the abdominal wound was reopened, but only capillary ooze of the type seen in heparinization was found. A small leak was discovered in the femoral arteriorraphy line. After this there was no further bleeding, but the patient's general condition remained critical. Despite the administration of oxygen, serum albumin, and a host of drugs, she died 48 hours after operation, apparently of heart failure. There was no autopsy.

Comment.—This was our second experience with the untoward effects of an anticoagulant given in conjunction with an operative procedure. Although the bleeding did not affect the outcome, it was a disturbing complication. The type of aortotomy done in this patient was easy to perform and effective in removal of the clot.

Case 4 (Fig. 4).—M. B., Hosp. 11276, a 57-year-old housewife, had suffered from rheumatic heart disease, mitral stenosis, and insufficiency for several years. She was frequently in failure and had been admitted twice before for digitalization, a course of mercurials, and rest. On Dec. 9, 1953, she was admitted for the third time, with a history of sudden onset of abdominal pain, two hours before, followed

Fig. 4 (Case 4).—Embolectomy incision is in the right common iliac artery.

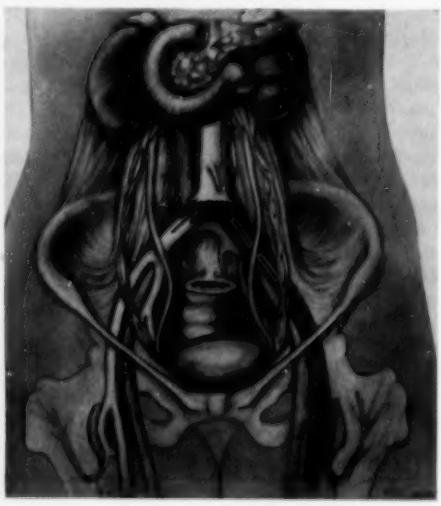
Fig. 5 (Case 5).—Note the low-lying duodenum overhanging the aortic bifurcation. The left common iliac artery is unusually long.

soon thereafter by weakness of the inferior extremities. Physical examination revealed a cyanotic, dyspneic middle-aged woman in obvious shock, with no peripheral pulses and weak heart action. There were scattered rhonchi at both lung bases. The heart was enlarged to the left; the sounds were weak and irregular, at a rate of 126. The inferior extremities were cold and mottled, with loss of sensation below midthigh. There were no pulses and no oscillometric readings. The lower abdomen was dusky but unusually warm down to the inguinal creases, where there was an abrupt temperature change. The pulsation of the abdominal aorta could be felt above the umbilicus. Despite her desperate state, it was felt that her only chance lay in operation. After two hours of oxygen, emergency digitalization, aminophylline, and morphine, a right iliofemoral incision was made with the patient under local anesthesia. Through this, with retroperitoneal dissection, the bifurcation of the aorta was exposed and the site of embolus isolated. The entire clot was removed through an incision in the right common iliac artery, as later proved at autopsy. As the wound in the skin was being closed, the patient suddenly died. Autopsy also disclosed the presence of chronic cardiac valvular disease, mitral stenosis, and insufficiency. The cause of death was heart failure.

Comment.—The question arises as to whether so desperately sick a patient should be operated upon. The answer is that intervention was her only hope. So-called conservative treatment, if the patient should improve somewhat, can lead only to gangrene of the extremities and an unhappier death. The descriptions of recovery from aortic embolism after conservative treatment are singularly unconvincing. They represent either cases of marked spasm with an incorrect diagnosis or those in which additive minor embolism has occurred in patients with previously obliterated pulses due to earlier embolism or arterial disease.

Case 5 (Fig. 5).—W. H., Hosp. 11796, a 36-year-old furrier, was admitted for the second time on Sept. 9, 1953. He had been known to have a murmur and enlarged heart for 20 years. Hemoptysis, nocturnal dyspnea, and racking cough had bothered him for three years. In the preceding two months, he had suffered cerebral, popliteal, and mesenteric embolisms. Two weeks after admission, there was a sudden onset of abdominal pain radiating into the extremities, which quickly became cold, mottled, and insensitive. Physical examination revealed an aphasic, dyspneic young man with an enlarged heart, murmurs at the apex, an irregular pulse, and pale, pulseless, insensate inferior extremities. With the use of general anesthesia, both femoral arteries were exposed and found to be collapsed, and serrefines were applied. The abdomen was entered through a lower midline incision. The third part of the duodenum came down to the fourth lumbar vertebra and overhung the bifurcation of the aorta.

Fig. 6 (Case 6).—Note the enormous amount of embolic material and propagated clot filling up the main left arterial trunk.



For this reason, an opening was made in the left common iliac artery, which was unusually long and divided at right angles into the hypogastric and external iliac. Clearance seemed to be effected, but when this site was closed the flow was unsatisfactory, and further arteriotomies in the external iliac and two more in the femoral were necessary. The latter proved troublesome, since an atheroma was cut through, the media split, and the endothelium stripped. Pulsation was established, but there was no doubt of the narrowing at the spot where the vessel was diseased. On the right side, all the clot was easily extruded through a common iliac incision. Postoperatively the right inferior extremity was warm with pulses but the left was cold below the knee. Seven hours later, the patient was returned to the operating room, and through two additional short femoral arteriotomies, a good spurting flow was obtained. However, it was apparent after 36 hours that the left leg was lost, and 10 days later, it was amputated below the knee. The patient did fairly well until the 13th day, when another embolus lodged in the right femoral artery, with additional cerebral embolism, and he died on the 14th day. Autopsy revealed rheumatic disease with mitral stenosis, a fresh clot in the right femoral artery, and old material in the left iliac artery.

Comment.—The two chief disadvantages of indirect embolectomy are demonstrated here, i. e., incising of diseased artery and failure completely to remove packed, tenacious clot.

Case 6 (Fig. 6).—B. G., Hosp. 35003, a 47-year-old housewife, was admitted on Feb. 13, 1954. She had been a chronic rheumatic cardiac patient who had done fairly well except during her two pregnancies. She had been in bed for the previous 10 days because of chest pain, fever, and hemoptysis. Twenty-two hours previously she had suddenly felt severe pain in both thighs and legs and her inferior extremities had become cold and insensate. On physical examination the heart was enlarged, the pulse was grossly irregular, and there were systolic and diastolic murmurs at the apex. There were neither pulses nor oscillations in the inferior extremities, the left particularly appearing cold and lifeless from upper thigh down. With the patient under general anesthesia, the femoral arteries were exposed and found pulseless; serrefines were applied. The incisions were carried cephalad, retroperitoneally. On the right, the clot was removed through a common iliac arteriotomy. On the left, multiple arteriotomies up to the bifurcation of the aorta were necessary to obtain a good flow. Since the legs still seemed cold, a right popliteal incision exposed a pulseless artery which was opened and probed, and a clot was removed before good flow was obtained and maintained. As the patient was turned to expose the left popliteal area, she suddenly became pulseless and the operation was terminated. By the 4th day after operation it was evident that the left inferior extremity was lost, and a midthigh amputation was performed on the 11th day. The right inferior extremity did well, with restoration of pulses, but there was a residual foot drop (peroneal) and ulceration in the lateral crural area. The patient was discharged five weeks after operation.

Comment.—Blood flow on the right was not reestablished until the expiration of 26 hours after the occlusion. It is significant that the extremity was saved. The prognosis in regard to recovery from the peroneal palsy is uncertain, but this can be taken care of by a foot-drop brace. The retroperitoneal approach was used because of the condition of the patient.

Fig. 7.—Schema of desirable operative plan. Serrefines are first placed on the femoral arteries to prevent embolic material from being swept down. Aortotomy is performed in the concavity of the bifurcation.

SUMMARY

On the basis of six personal cases there is presented a schema of operative attack for aortic embolism.

When the condition of the patient permits, exposure and clamping of the femoral arteries followed by direct transabdominal aortotomy is the procedure of choice for the treatment of embolus at the bifurcation of the aorta.

If the indirect, retroperitoneal approach is used, care must be taken not to incise through sites of arterial disease. Arterial clearance must be carefully established, since it is possible to leave fragments of clot which

subsequently block the lumen, despite a free, spurting flow of blood.

General or local anesthesia in combination are preferable to spinal. The use of anticoagulants is to be avoided. Serious bleeding occurred in the two cases in which depot heparin was given.

The anatomic level of the bifurcation, the relative length of the common iliac arteries, and the presence of horseshoe kidney or low-lying duodenum are factors of technical importance.

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CONSTRUCTION OF FRESH AUTOGENOUS ARTERIAL GRAFTS

III. Concluding (Three-Year Survival) Studies on Splenic Artery Fabricated Grafts in Aorta

ELLIOTT S. HURWITT, M.D., and ADRIAN KANTROWITZ, M.D., New York

AN EXPERIMENTAL program was initiated in this laboratory in November, 1950, to investigate the feasibility of bridging a gap in the aorta by a graft fabricated from segments of an expendable autogenous artery. Preliminary observations, including one-year survival studies reported before this society, indicated satisfactory functional and anatomical results. Biological superiority over homografts or heterografts, either fresh or preserved by any of the available methods, was attested by survival of the muscle cells and elastic laminae of the media, with no evidence of calcification.* Two dogs maintained for three years with similar grafts form the basis for these concluding observations.

From the Surgical Research Laboratories, the Montefiore Hospital.

Presented at the Second Scientific Meeting, The International Society of Angiology, North American Chapter, San Francisco, June 19, 1954.

* References 1 and 2.

EXPERIMENTAL METHOD

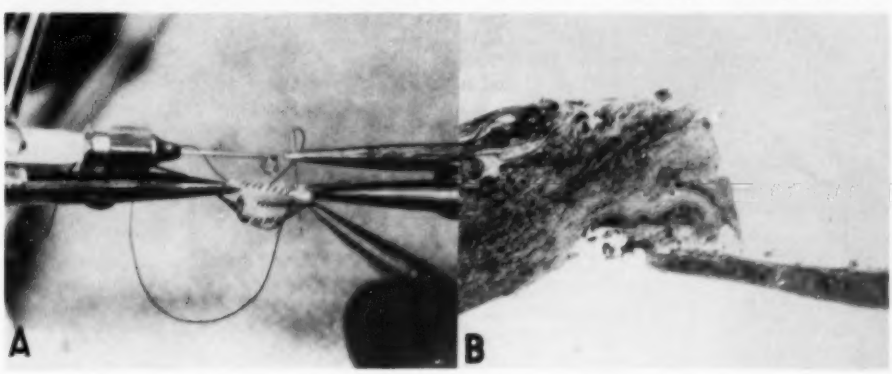
The method has been amply described and illustrated in the publications previously referred to. In a series of large mongrel dogs, a generous length of splenic artery was resected, incised longitudinally, and divided transversely into equal segments. The lateral margins of these panels were sutured together, creating a tubular structure which was interposed between the transected ends of the abdominal aorta after removal of an aortic segment (Fig. 1). The graft was wrapped with compressed absorbable gelatin sponge (Gelfoam),† gentle compression maintained until hemostasis had been achieved, and the abdominal wall closed in layers.

EXPERIMENTAL RESULTS

Eighteen grafts, of a total of 30 experiments, were available for pertinent survival observations. Patency was documented both by adequate function and palpable femoral pulsations and by retrograde aortography performed in the early postoperative period

† Supplied through The Upjohn Company, Kalamazoo, Mich.

Fig. 1.—*A*, construction of fabricated graft nearing completion; *B*, disparity in thickness between splenic artery and aorta. Hematoxylin and eosin stain; reduced ¼ from Mag. × 25.



and shortly before killing of the animal. The status of the graft was evaluated at autopsy by gross and microscopic study. An analysis of the 12 failures and the salient features of 16 of the 18 satisfactory specimens obtained from staged survival studies up to one year after operation are contained in the earlier reports from this laboratory. Late thrombosis, delayed rupture, or calcification were not encountered. Endothelialization of the intimal surface, a layer of subintimal fibrosis of variable thickness, a relatively intact media, and a dense vascularized adventitia from organization of the absorbable gelatin sponge were the consistent findings. The observations in the two dogs maintained for three-year survival periods are now available for comparison.

Dog H-6-51: A 46 lb. (20.9 kg.) middle-aged male, Labrador retriever type, with long black hair. Date of operation, Jan 26, 1951; date of killing, Jan. 6, 1954. The resected length of splenic artery measured 45 mm. in length and 7 mm. in circumference, in the relaxed state. Three panels, each 15 mm. long, were fashioned into a tubular graft which replaced a 10 mm. segment of the abdominal aorta. In situ, the dimensions of the graft were: length, 24 mm.; diameter, 10 mm.—equal to that of the host aorta.

The immediate postoperative course was uneventful. Retrograde aortography was performed on the 55th and the 1,076th days after operation (Fig. 2*A* and *B*). The early films showed excellent visualization of the graft, which was smaller in caliber than the host, with slight narrowing at each horizontal suture line. An increased narrowing is apparent at the proximal anastomosis in the final roentgenograms, which also show no dilatation of the graft, and slight dilatation of the aorta below the graft. The dog aged perceptibly during the third year of observation, had four minor convulsive episodes, and periodically lost much of his coat. At the time of killing on the 1,076th day, he weighed 50 lb. (22.7 kg.) and was in good condition.

The graft was minimally adherent to the inferior vena cava, with little periaortic fibrosis or inflammatory reaction. No absorbable gelatin sponge was grossly identifiable. The circumference of the excised aorta measured 19 mm. above and 20 mm. below the graft. The proximal suture line measured 16 mm. and the distal suture line 17 mm. in circumference. In the midportion of the graft the circumference was 13 mm. All of the suture lines were covered by a slightly cloudy shiny layer of tissue which varied considerably in thickness in different portions of the graft. Two small shallow healed ulcerations were present in the graft, and there were "clamp marks" in the aorta proximally and distally (Fig. 2*C*). There were no thrombi, atherosclerotic deposits, or calcification.

Sections of formalin-fixed material were prepared with hematoxylin and eosin, Masson, and

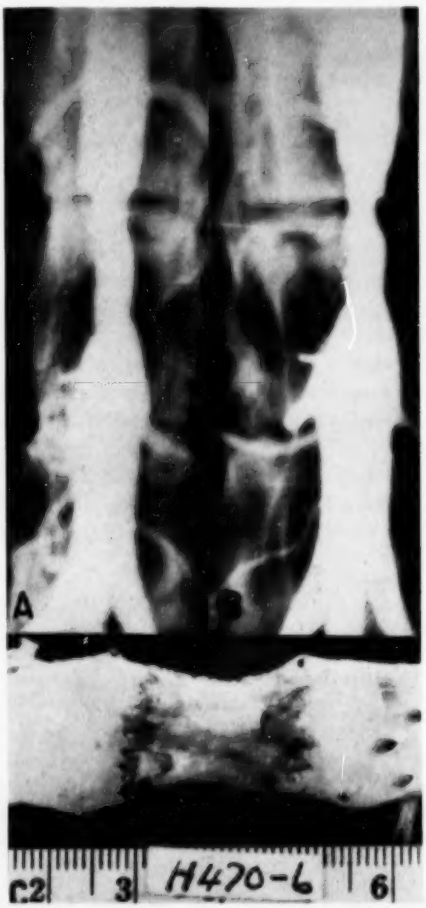


Fig. 2.—Dog H-6-51. *A* and *B*, retrograde aortograms 55 and 1,076 days respectively postoperatively; *C*, gross appearance of specimen on 1,076th day.

elastica Van Gieson stains. Grossly and microscopically, the graft was similar in thickness to the aorta. Beneath a thin layer of endothelial cells was a moderately dense subintimal zone of fibrosis which was wider in some areas than in others. The muscle cells of the media showed a substantial proportion of survival, and the laminae of

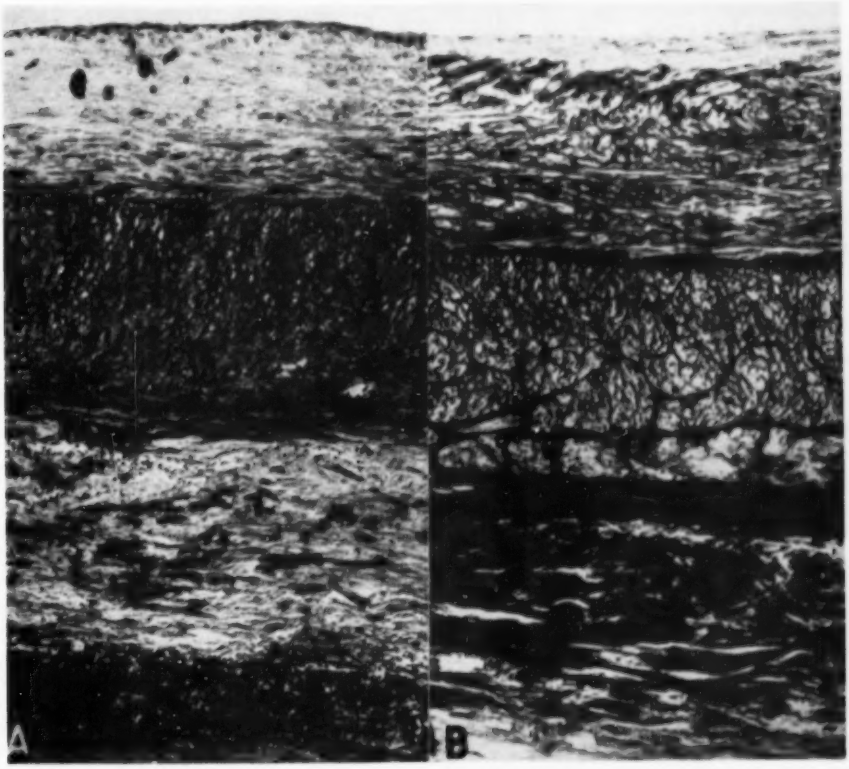
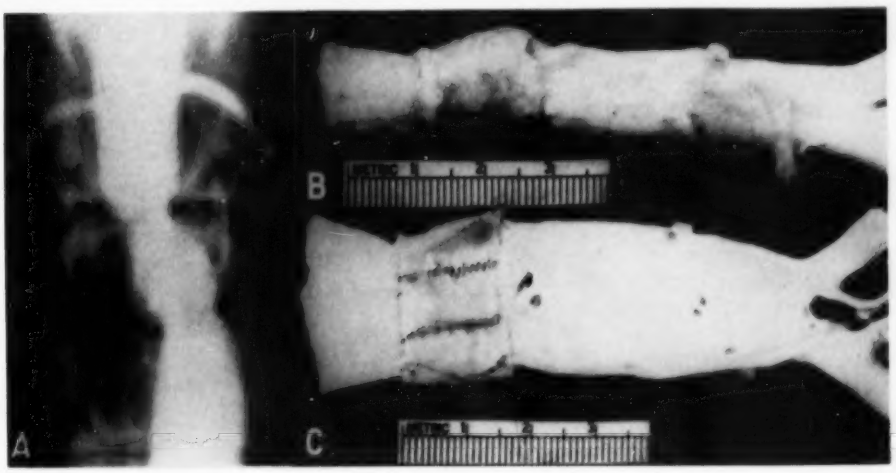


Fig. 3.—Dog H-6-51. Photomicrographs of specimen with Masson (*A*) and elastica Van Gieson (*B*) stains showing subintimal fibrosis, survival of muscular and elastic tissue elements of media, and thick vascular adventitia from organized absorbable gelatin sponge, reduced ¼ from Mag. × 150.

Fig. 4.—Dog H-18-51. *A*, retrograde aortogram 1,098 days postoperatively; *B* and *C*, gross appearance of specimen on 1,104th day.



elastic tissue were well preserved (Fig. 3). The width of the media was variable, and neither this nor the degree of integrity of the muscle cells could be correlated with the extent of overlying subintimal fibrosis. A dense, vascular adventitia was present, with small nutrient vessels on both the medial and adventitial sides of the external elastic layer. A minimal foreign-body reaction was noted in proximity to the suture material.

Dog H-18-51: A 90 lb. (40.8 kg.) elderly male, giant beagle type. Date of operation, March 30, 1951; date of killing, April 7, 1954. The resected segment of splenic artery measured 55 mm. in length and 7 mm. in circumference in the relaxed state. Three panels, each 18 mm. long, were fashioned into a tubular graft; the graft was 19 mm. long after it had been sutured into place. The outside diameter of the pulsating aorta measured 13 mm., and the resected segment of aorta had a circumference of 25 mm. This was the largest dog in the series, and the size of the pertinent structures greatly simplified the technical details of the operation.

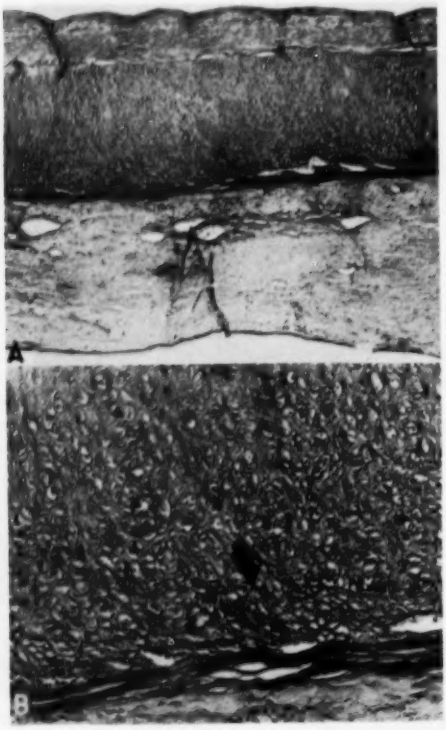


Fig. 5.—Dog H-18-51. Photomicrographs of specimen showing integrity of graft. Masson stain reduced ¼ from Mag. (*A*) × 85 and (*B*) × 250.

The entire postoperative course in this sedate animal was without incident. Retrograde aortography initially was unsuccessful for technical reasons. Films obtained on the 1,098th postoperative day show a smoothly outlined, patent, somewhat angulated graft, equal in diameter in its midportion to the caliber of the aorta, with slight narrowing at each anastomosis (Fig. 4*A*).

At the time of killing, 1,104 days postoperatively, the dog weighed 82 lb. (37.2 kg.) and was in fine condition, although quite old. The graft presented a sinuous appearance, but the narrowing at the suture lines was less pronounced than in the roentgenograms (Fig. 4*B*). The aorta separated readily from the adjacent structures. The graft measured 18 mm. in length. The following measurements of circumference were obtained: proximal anastomosis, 23 mm.; body of graft, 27 mm.; distal anastomosis, 25 mm.; aorta above and below graft, 29 mm. The longitudinal suture lines were clearly visible beneath a thin endothelial layer, which was considerably more homogeneous and less dense than in the preceding specimen (Fig. 4*C*). A 2-mm. yellow shallow ulceration was present near the midportion of one of the panels, and there were no thrombi or calcific deposits.

The microscopic findings were similar to those in the graft from dog H-6. The area of subintimal fibrosis was considerably thinner, but variable. Survival of the muscle cells and elastic fibers of the media was present, with minimal increase in fibrous tissue. The vascular newly-formed adventitia resulted in a graft comparable in thickness to that of the aorta (Fig. 5).

COMMENT

The survival of the muscular and elastic tissue components of the media of fabricated fresh autogenous arterial grafts has been corroborated by Sandblom and his colleagues,‡ Potts and co-workers,[5] and Schmitz and his co-workers.[6] These groups employed the iliac, femoral, and subclavian arteries, respectively, as the sources of supply. The method of constructing the "compilation autograft" [6] was similar for all three groups, by a circular rather than the lateral technique described in reports from this laboratory, gaining diameter at the expense of length. The functional and histologic results were the same despite these technical differences. Kanar and others [7] have demonstrated, in pigs, that aortic homografts to the thoracic

‡ References 3 and 4.

aorta show greater degenerative changes than do those to the abdominal aorta. The site of implantation made little difference in the survival of the media in the autografts under discussion. In none of the other studies has the reported survival period been extended to the duration indicated in the present series.

The large arteries utilized in other laboratories for fabricated aortic grafts have the unique advantage of an arterial wall of substantial thickness, in contrast to such expendable vessels as the splenic or internal mammary arteries. On the other hand, the iliac or femoral arteries would hardly be available for human application, and sacrifice of the subclavian artery during operation for coarctation of the aorta may jeopardize important components of the collateral bed and the actual viability of the arm.[8] The disparity in thickness between the splenic artery and the aorta has consistently been overcome in this series by the use of absorbable gelatin sponge (Gelfoam), as is evident by comparing Figure 1*B* with Figures 3 and 5. Progressive organization of absorbable gelatin sponge under these circumstances into a strong, vascular connective tissue backing for the graft has previously been documented in this laboratory.[9]

It had originally been planned to conclude this investigation after survival periods of 18 to 24 months. Subsequently, during a general discussion of vascular grafts, it was pointed out that some of the experimental aortic homografts had demonstrated delayed thinning of the wall with significant dilatation, and it was suggested that these dogs be maintained for an additional interval.§ No suggestion of aneurysmal dilatation, thinning of the wall, calcification, or late thrombosis was encountered in the fabricated autografts. The graft in dog H-6-51 was obviously smaller than the aorta initially, and a four-panel graft would probably have been preferable. The superiority of periodic aortography over anatomical dissections in the functional evaluation and visualization of the shape of a vascular graft has again been substantiated in this study.

A limited appraisal of human autopsy material was undertaken ‖ to evaluate a possible clinical application of this technique, and this has been described in some detail

§ Deterling, R.: Personal communication to the authors.

‖ By Dr. Stanley Altman, through the courtesy of Dr. Harry M. Zimmerman, Chief of the Laboratory Division, the Montefiore Hospital.

Fig. 6.—Segments of human thoracic and abdominal aorta and splenic artery.

in the earlier publications.¶ A sufficient length of the enlarged internal mammary artery of an adult with coarctation of the aorta was available for the construction of an adequate graft. The comparative dimensions of the thoracic aorta, abdominal aorta, and splenic artery in a routine postmortem examination are illustrated in Figure 6.

The outstanding feature of the fabricated autografts has been the survival of the media, in contrast to the fibrous tissue replacement, collagenous degeneration, and occasional calcification observed in homografts and heterografts. Whether or not this constitutes an advantage that would be desirable for clinical application remains to be considered. The major drawback to the method is the time required to construct the graft, which may be minimized by simultaneous dissection of the vessel to be replaced by another team. The technique is obviously unsuited to the situation in which a long gap requires bridging, because of limitations in available autogenous material. The prolonged survival without degenerative changes of these grafts in older dogs constitutes a critical biologic test. Growth of such grafts when inserted in puppies has also been described.[6]

Gross has recently summarized his experiences with the use of preserved aortic homografts in the correction of 46 cases of coarctation of the aorta in the past six years.# Calcification in the graft had been demonstrable in three instances by roentgenographic study, and he reported no examples of aneurysmal dilatation. The unique observation that a single aortic homograft, out of an extensive series in pigs, has manifested survival comparable to that of the autografts[7] should stimulate a continued investigation of the paramount aspect of the problem concerned with a biologic specificity of foreign proteins.

SUMMARY

Three-year survival studies have been recorded on grafts fabricated from autogenous splenic artery segments and inserted in the abdominal aorta of dogs.

Preservation of the integrity of the media of these grafts is consistent with that reported previously from this laboratory in shorter term studies and corroborated by others.

These grafts are as satisfactory functionally as homografts or heterografts and they are superior biologically.

Clinical applications of this method are suggested.

The conversion of blood-soaked absorbable gelatin sponge to organized connective tissue under the conditions of these experiments has again been demonstrated.

Gross, R. E., in discussion of Kanar et al.[7]

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FAILURE OF POLYETHYLENE WRAPPING IN TREATMENT OF AORTIC ANEURYSMS

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THE VARIOUS procedures which have been proposed and used in the surgical treatment of aneurysms of the aorta have been classified into three major categories: (1) those designed to promote thrombosis and fibrotic organization by partial, complete, or gradual occlusion or ligation of the aorta, by the introduction of foreign material, or by the stimulation of periarterial fibroblastic reaction; (2) endoaneurysmorrhaphy, and (3) extirpation of the lesion.* Among the first group the use of cellophane or polyethylene wrapping has gained considerable popularity in recent years, owing probably to its relative ease and safety of application. The essential basis for its usefulness lies in certain experimental evidence of its ability to promote fibrosis. Clinically, however, its efficacy has not been well established and has actually been questioned.† For this reason it seems desirable to report our experience with eight cases in which this method of therapy was employed and in which resection was subsequently performed.

The irritating properties of cellophane were originally indicated in 1939 by Page,[25] who, during the course of experiments on hypertension, wrapped the kidneys of dogs in cellophane bags to prevent formation of collateral blood supply and at subsequent necropsy observed that the kidneys were shrunken and encased in a dense fibroblastic and collagenous layer 0.4 cm. in thickness. On the basis of these observations, Pearse [26] in the following years employed cellophane as an experimental means of gradual occlusion of large arteries. Ordinary Du Pont cellophane No. 300 T. was soaked in alcohol or a solution of mercuric cyanide for 12 hours, folded into a strip four layers thick, and loosely wrapped three times about the aorta or carotid artery of dogs. Pearse noted in 24 experiments that cellophane was a tissue irritant and that extensive changes occurred in the vessels treated in all but two animals. The reaction consisted in a partly hyalinized fibrocollagenous layer containing many phagocytic cells and purulent or gelatinous fluid in its center. Progressive constriction of the vessel with obliteration of the lumen had resulted in some instances.

These encouraging experimental observations led Harrison and Chandy,[17] in 1943, to employ the procedure in the treatment of two patients with aneurysms of the subclavian artery. In one of these, there was questionable clinical evidence that this caused reduction in the size of the aneurysm, and in the other wound suppuration occurred and the operation was a failure. In the same year there appeared reports of the use of the procedure in operations for obliteration of patent ductus arteriosus.‡

In the meantime, other investigators § found that cellophane was an inert substance and reported its successful use in preventing adhesions following arthroplasty, synovectomy, and certain tendon operations. Moreover, Giles,[18] in 1942, reported observations

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Supported in part by grants from the Houston District Chapter, Texas Heart Association, and the Cora and Webb Mading Fund for Surgical Research.

Presented at the meeting of the International Society of Angiology, North American Chapter, June 19, 1954, San Francisco.

* References 5 and 22.

† References 6 and 9.

‡ References 14 and 16.

§ References 3, 12, 15, 23, and 32.

in direct conflict with those previously recorded by Pearse.[26] He found that in none of seven dogs in which the abdominal aorta was wrapped with cellophane for varying periods up to one year in a manner similar to that used by Pearse was there any evidence of occlusion or even the slightest constriction of the aorta.

These conflicting observations regarding the properties of cellophane were partially resolved by Poppe and de Oliveira,[28] who discovered that two types of material had been employed: cellophane and cellulose film, and polyethylene, a plastic film. Two to ten weeks after they wrapped polythene and cellophane about the abdominal aorta of dogs, they observed a dense fibrous tissue response to the polyethylene, whereas there was little reaction to the cellophane. They concluded that cellophane is inert and polyethylene film reactive. The principal differences between polyethylene and cellophane were further elucidated by Ingraham, Alexander, and Watson.[21] Shortly thereafter, Yeager and Cowley [34] pointed out that there were two forms of polyethylene, namely, the pure form which is made by extruding the melted material as a film, and is inert, and the impure form which is prepared by casting from a solution onto rollers and contains less than 1% of dicetyl phosphate. It was this latter substance, they concluded, and not the plastic material itself that was responsible for the tissue reaction produced by polyethylene film. They suggested that a similar result in treatment of aneurysms could be obtained by use of dicetyl phosphate alone, since polyethylene film might retard the process of wound healing. After this study identifying dicetyl phosphate as the fibrogenic agent and thus making possible the selection of cellophane-polyethylene films having more consistent fibroblastic response, the method gained considerable popularity and several observers reported encouraging results with its use in the treatment of aneurysms of the aorta, particularly in the form of palliation.‖

‖ References 1, 4, 7, 8, 11, 18, 19, 20, 24, 27, 29, 30, 31, and 33.

There has been little evidence, however, other than clinical impressions and symptomatic improvement to support the belief that the method has actual curative value. Indeed, Abbott found from his analysis of 32 patients with thoracic aneurysms treated in this manner that life was not prolonged in any with advanced disease and that the only beneficial result was relief of pain in about 40% of the cases. Moreover, there has been a paucity of morphologic examinations of the wrapped aneurysms at subsequent operation or at necropsy. Examination of an aneurysm of a pulmonary artery by Abbott [1] eight days after it was wrapped with polyethylene film revealed fibroblastic reaction in the areas in contact with the cellophane, not merely around the aneurysm but also about the overlying pericardium and a portion of the left atrium. He wrapped another aneurysm of the descending portion of the aortic arch with polyethylene, and at necropsy, two and one-half months later, there was evidence that the aneurysm had leaked and displaced the polyethylene from its original site of application. There was slight reactive thickening of the wall, which was attributed to early interposition of a hematoma between the aneurysmal wall and the overlying polyethylene or to retention of the cellophane in alcohol for several weeks prior to use.

In a case of an abdominal aortic aneurysm coming to necropsy 25 days after treatment by cellophane wrapping, Croot [8] observed about the aorta an inflammatory reaction which was considered greater than at operation. The pieces of cellophane had slipped upward and downward from the crown of the aneurysm, and each cellophane piece lay within a shallow space of fibrous tissue with a smooth lining. The fibrous tissue was three or four times thicker over the most prominent part of the aneurysm not wrapped with cellophane than over the adjoining cellophane-covered portions. Microscopic examination disclosed relatively slight fibrosis in the areas that were in direct contact with the cellophane.

Of 12 patients with aortic aneurysms treated by polyethylene wrapping, Hume [20]

reported microscopic observations in only one of four examined at necropsy. In this instance, the media and adventitia were replaced by a hyaline type of connective tissue with vascular spaces and round-cell infiltration.

Cowley and Yeager [7] described the microscopic findings in 1 of 37 patients with aneurysms of the aorta and great vessels, most of whom were treated by polyethylene wrapping. The adventitia of the vessel beneath the polyethylene had been replaced by hyalinized connective tissue. At necropsy on another of these patients, the wrapped aneurysm appeared to be encased in scar tissue.

Thus, while it has been demonstrated in experimental animals that polyethylene film containing dicetyl phosphate produces a fibrous tissue response, the evidence of its clinical value and efficacy in the treatment of aortic aneurysms is far from convincing. Our experience with eight cases of aneurysms of the abdominal aorta previously treated by polyethylene wrapping and subsequently resected provided an opportunity to make certain morphologic studies as well as clinical observations on the effects of the procedure, thus permitting a more critical evaluation of this method of therapy.

Polyethylene (Du Pont Polythene N. V. 7-14) containing dicetyl phosphate was used in all the cases. Sterilization was obtained by soaking the sheets of polyethylene in a solution of 1 to 1,000 aqueous cetylpyridinium (Zephiran) chloride for at least 30 minutes prior to use. The interval between the wrapping procedure and subsequent resection of the aneurysm varied from 7 to 41 months. The procedure employed at the second operation consisting of resection of the aneurysm with replacement by an aortic homograft was essentially similar to that previously described.[9] Comparative observations were made of the relative dimensions and character of the aneurysms at the time of the initial operation and the subsequent resection. Gross and microscopic studies were also made, particularly to compare areas of the wall covered by polyethylene with those not in contact with this material. Paraffin sections were taken from representative portions of the covered and uncovered areas and were stained with hematoxylin and eosin and Masson's trichrome stain. In addition to the usual microscopic examination, the slides were also examined under polarized light in order to better identify the presence of the polyethylene.

REPORT OF CASES

CASE 1.—R. H., a 55-year-old white man, was first admitted to the Methodist Hospital on Dec. 28, 1949, with a history of dull, aching, intermittent pain in the left lower quadrant and back for two and one-half years. Physical examination revealed a large pulsating mass in the midabdomen.

On Dec. 30, 1949, abdominal exploration disclosed a fusiform aneurysm of the aorta arising just below the renal arteries and extending down the aortic bifurcation measuring about 9 by 12 cm. The aorta was mobilized just above the aneurysm, and a No. 18 rubber catheter wrapped in reactive polyethylene film was passed about the aorta and tied so as to reduce the lumen by approximately two-thirds. After this, pulsations in the aneurysm were significantly reduced. A sheet of polyethylene was then placed over the anterior and lateral walls of the aneurysm and fixed with several interrupted sutures. The patient recovered from the operation satisfactorily and was discharged Jan. 9, 1950. Although there was some relief of symptoms during the first six months after operation, there was gradual return of his previous symptoms, with several episodes of rather severe lower abdominal and back pain.

He was readmitted on May 24, 1953, because of progressively severe abdominal and back pain and increase in the size of the abdominal mass. Upon examination, the aneurysm appeared to have increased, and roentgenograms of the abdomen disclosed the aneurysm with calcific change in its wall. Operation, on May 26, 1953, revealed that the aneurysm had increased to approximately twice its size at the initial operation, 41 months previously, and now extended downward to include the bifurcation of both common iliac arteries. Further dissection showed that the aneurysm had eroded the fourth lumbar vertebra. The aneurysm was excised, and the defect was bridged with an aortic bifurcation homograft. On the right the anastomosis was made to the external iliac artery, as the internal iliac was destroyed by the aneurysm. On the left the anastomosis was made to both internal and external iliac arteries. Convalescence was uneventful, and the patient was discharged June 4, 1953.

The specimen removed consisted of a large fusiform aneurysm of the abdominal aorta, including the bifurcation and both common iliac arteries, measuring 19 cm. in length and 12.5 cm. in diameter. The adventitial surface was smooth, gray, pink, and glistening. The sac contained a laminated clot with an intima-like, smooth, pink, inner lining. At the upper margin a portion of a catheter was evident,

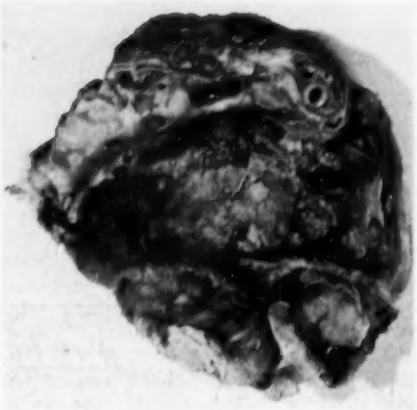


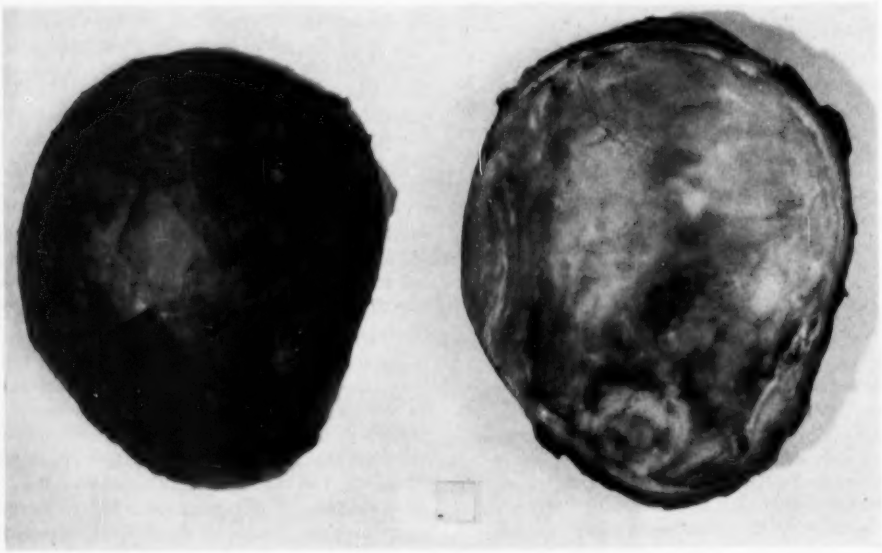
Fig. 1.—Resected aneurysm of the abdominal aorta (Case 1) 41 months after it was wrapped with polyethylene and the aorta just proximal to the aneurysm constricted with a polyethylene-wrapped rubber catheter. The aneurysm has enlarged and now includes the catheter that has eroded the wall and projects into the lumen.

Fig. 2.—Microscopic preparation from the wall of the aneurysm (Case 1) with tissue reaction about the polyethylene film viewed through polarized light. The polyethylene appears as an isotropic substance, and it is surrounded by a thin layer of dense hyalinizing fibrous connective tissue with occasional giant cells of the foreign body type; reduced 3/10 from Mag. × 30.

about which there was also some Cellophane material embedded in the wall. In one area the catheter had eroded through the wall into the lumen of the aorta (Fig. 1).

Microscopically, the thrombus attached to the inner surface contained many slit-like spaces and was contiguous to areas of atheromatous change containing foam cells. Collagenous bundles, in places spread apart by extravasated erythrocytes, contained streaks of connective tissue about the vasa vasorum

Fig. 3.—Resected aneurysm of the abdominal aorta 33 months after it was wrapped with polyethylene (Case 2). On the anterolateral surfaces over the polyethylene there is a thin film of fibrous connective tissue. On cut surfaces the wall of the aneurysm is 0.2 to 0.5 cm. thick and the lumen is filled with a laminated thrombus.



that were infiltrated by lymphocytes, plasma cells, and large mononuclear cells. The aggregations of lymphocytes in some places amounted to the formation of follicles. In the area adjacent to the polyethylene there was a condensation of fibrous connective tissue and focal areas of reaction with giant cells of the foreign body type (Fig. 2).

Case 2.—L. B., a 75-year-old white man, was admitted to the Hermann Hospital on Oct. 11, 1951, complaining of pain in the right upper quadrant of the abdomen of several months' duration. Physical examination revealed a pulsating mass in this region of the abdomen, and an aortogram confirmed the diagnosis of an aneurysm of the abdominal aorta arising well below the renal arteries and extending down to the bifurcation.

On Oct. 17, 1951, laparotomy revealed the aneurysm arising at about the level of the inferior mesenteric artery and measuring about 8 by 10 cm. After the aneurysm was freed on its lateral and anterior surfaces from the surrounding tissues, these surfaces were covered with a sheet of re-

Fig. 4.—Microscopic preparation from the wall of the aneurysm (Case 2). The outer surface adjacent to the polyethylene is composed of dense hyalinizing fibrous connective tissue with infiltrations about vasa vasorum of lymphocytes, plasma cells, and large mononuclear cells; reduced ½ from Mag. × 50.

active polyethylene film and sutured in place. This was then covered by the overlying posterior peritoneum and the wound closed in layers.

The patient was discharged from the hospital in good condition on Nov. 2, 1951. He was relieved of symptoms for about a year and then had gradual recurrence of pain. During the following year this became progressively worse, with some increase in size of the mass and he was forced to cease work.

He was admitted to the Methodist Hospital on July 5, 1954, because of sudden increase in size of the aneurysm as well as in severity of symptoms. Physical examination revealed the pulsatile mass in the right upper abdominal quadrant to be considerably larger than on his previous admission.

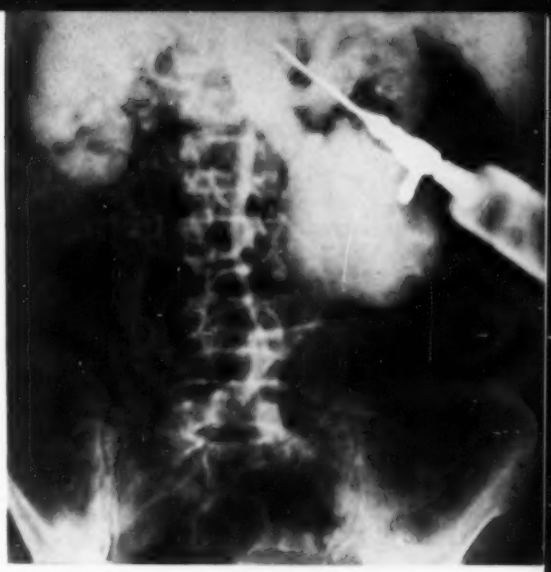


Fig. 5.—Translumbar aortogram (Case 3) prior to wrapping of aneurysm with polyethylene film. The aneurysm appears to be about 8 cm. in length and 6 cm. in diameter.

On July 7, 1954, approximately 33 months after the initial operation, the aneurysm was resected and replaced with an aortic homograft. The patient's postoperative course was uneventful and he was discharged from the hospital on July 17, 1954, completely relieved of symptoms.

The aneurysm measured 12.5 by 17 cm. The outer wall was glistening in places and revealed marked arteriosclerotic change. On cut section a firm, laminated gray-white thrombus filled almost the entire lumen of the aneurysm. Over the anterior and left lateral wall a layer of polyethylene film was discernible beneath a thin membranous layer (Fig. 3).

Microscopically, a partly organized thrombus lined the inner surface. Beneath this, atheromatous

Fig. 6.—Translumbar aortogram (Case 3) performed about 26 months after the aneurysm was wrapped with polyethylene film. It is evident from the aortogram and the excised aneurysm which has been superimposed that a significant increase in size of the aneurysm occurred after wrapping with polyethylene film.

areas were noted between coarse collagenous bundles. About the vasa vasorum there was loose connective tissue infiltrated by lymphocytes, plasma cells, and large mononuclear cells. A condensation of collagenous fibers was noted on the surface adjacent to the polyethylene (Fig. 4).

CASE 3.—J. B., a 66-year-old white man, was first admitted to the Jefferson Davis Hospital Feb. 3, 1948, with pain in the left upper quadrant of the abdomen. The presence of a pulsatile mass was confirmed, and he was discharged without surgical intervention.

Symptoms persisted and increased slightly in severity, until his second admission, Dec. 11, 1951, because of the onset of high lumbar back pain. Lumbar aortogram revealed an aneurysm of the abdominal aorta arising just below the renal arteries and measuring approximately 8 cm. in length and 6 cm. in diameter (Fig. 5).

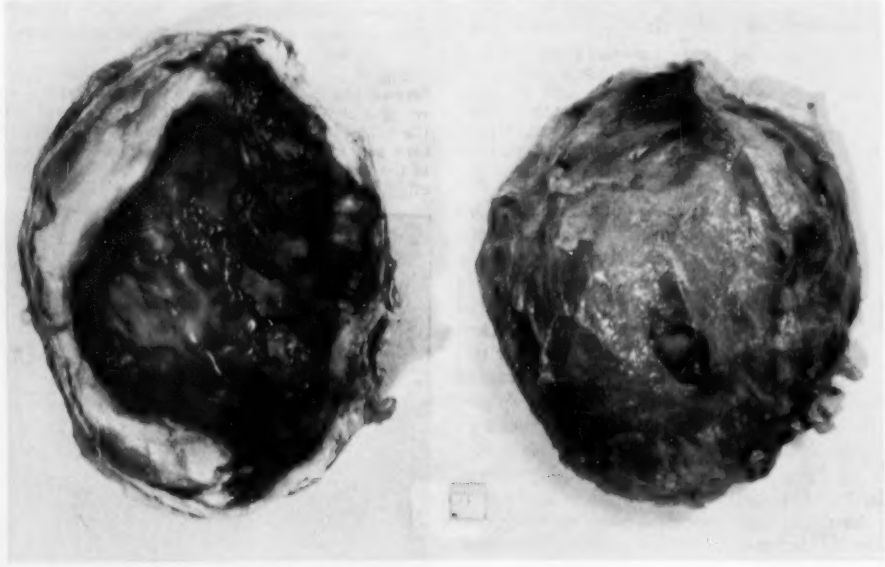
At laparotomy on Jan. 3, 1952, the aneurysm was mobilized and wrapped with reactive polyethylene film. After operation and for the next 12 months he was somewhat relieved of pain.

He was readmitted to the hospital on Feb. 17, 1954, complaining of a sudden increase in severity of abdominal pain and in size of the abdominal mass. Examination disclosed the abdominal aneurysm to be tender and filling the entire left upper abdominal quadrant. An aortogram revealed the aneurysm to have increased significantly in size since the first examination, 26 months previously (Fig. 6). At operation Feb. 25, 1954, the aneurysm was found to extend from a point just below the renal arteries distally to include the aortic bifurcation. The aneurysm was removed and a lyophilized bifurcation homograft was inserted. Convalescence was uneventful, and the patient was discharged from the hospital on March 25, 1954.

The specimen consisted of a large fusiform aneurysm of the abdominal aorta, measuring 12 by 10 cm. On its left lateral, its anterior, and part of its right lateral surface it was covered with polyethylene film over part of which there was a thin granular membrane (Fig. 7). Section revealed the lumen to be partly filled with a laminated thrombus (Fig. 7). In some places the wall was 0.5 to 1 cm. thick and elsewhere less than 0.2 cm. Immediately beneath the polyethylene film there was a delicate fibrous layer about 0.1 cm. in thickness.

Microscopically the anterior wall of the aneurysm revealed the inner surface to be covered by a thrombus contiguous in places to areas of extensive atheromatous change. The media and adventitia were replaced by coarse collagenous bundles with no elastic fibers discernible. On the surface there was a zone of hyalinized fibrous connective tissue that varied in width (Fig. 8). In the thinner posterior wall similar changes were noted, and, in addition, there were calcific deposits.

Fig. 7.—Resected aneurysm of the abdominal aorta 26 months after it was wrapped with polyethylene (Case 3). A thin film of fibrous connective tissue covers the polyethylene over the anterior and lateral surfaces. On cut surfaces the wall of the aneurysm varies from 0.2 to 0.5 cm. in thickness. A laminated thrombus is adherent to the inner surface of the anterior wall.



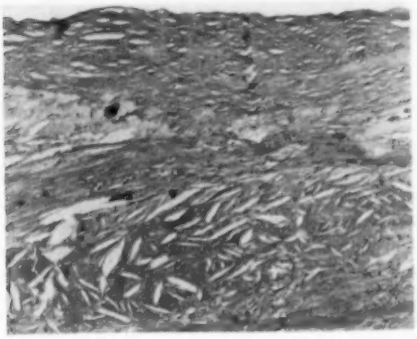
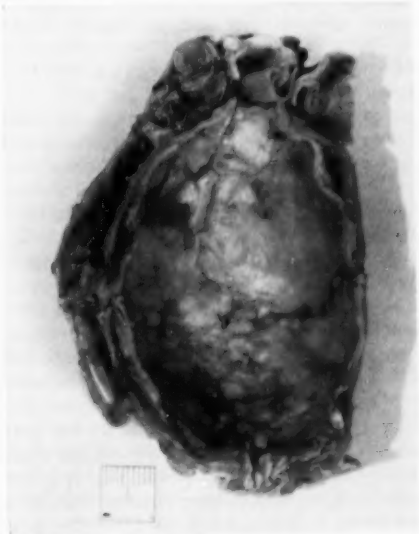


Fig. 8.—Microscopic preparation from the anterior wall of the aneurysm (Case 3). There is a thin layer of dense, hyalinizing, fibrous connective tissue on the external surface. Beneath this, atherosclerotic changes are evident; reduced ½ from Mag. × 100.

Case 4.—G. W., a 52-year-old white man, was admitted to Hermann Hospital on June 17, 1951, with mild abdominal pain. A diagnosis of abdominal aortic aneurysm was made. At operation on June 19, 1951, the aneurysm was found to arise just distal to the renal arteries and to extend to the bifurcation. It was fusiform in type and approximately 6 by 8 cm. in size. The aneurysm was mobilized, and the proximal aorta was partially occluded with a ligature made of a Penrose drain wrapped with reactive polyethylene film; then the aneurysm was wrapped on all surfaces except the posterior wall. He recovered uneventfully.

During the ensuing 23 months the abdominal discomfort increased slightly with a progressive increase in the size of the mass. He was admitted to the Methodist Hospital on May 21, 1953, and operation was performed five days later. The aneurysm, which had increased considerably in size since the initial operation 23 months previously, was removed, together with the bifurcation of the aorta, and a lyophilized bifurcation homograft was inserted into the defect. Convalescence was uneventful, and the patient was discharged on June 3, 1953.

Fig. 9.—Resected aneurysm of the abdominal aorta 23 months after it was wrapped with polyethylene and the aorta just proximal to the aneurysm constricted with a polyethylene-wrapped Penrose drain (Case 4). The anterior wall, covered by polyethylene, is slightly thickened. The posterior wall is thin, and separation of the layers of the wall is evident.



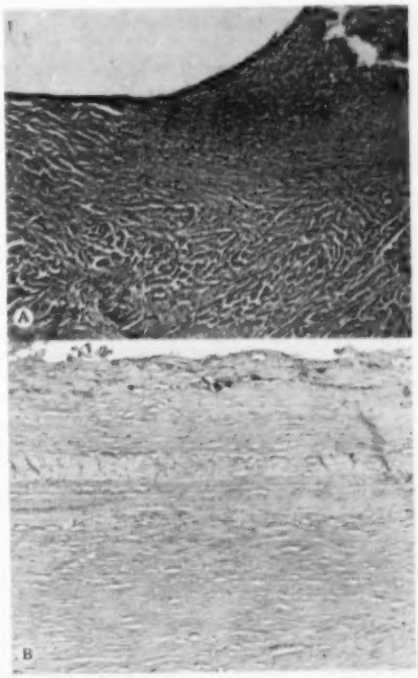


Fig. 10.—*A*, microscopic preparation from the wall of the aneurysm (Case 4) in the region of the polyethylene-wrapped Penrose drain. The reaction about the polyethylene consists of a layer of dense, hyalinizing, fibrous connective tissue with infiltrations of lymphocytes, plasma cells, and large mononuclear cells; reduced ½ from Mag. × 100. *B*, microscopic preparation from the posterior wall of the aneurysm (Case 4) which was uncovered by polyethylene film. The tissue reaction is similar to that noted on the anterior wall of the aneurysm in contact with polyethylene; reduced ½ from Mag. × 100.

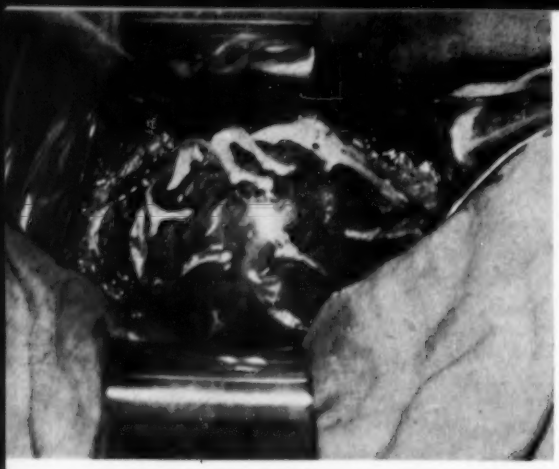


Fig. 11.—Photograph made at operation (Case 5) showing the size of the aneurysm at the time polyethylene film was applied to its surface.

The aneurysm measured 9 by 12 cm. The adventitial surface was gray pink and somewhat roughened in areas but not otherwise unusual. The polyethylene-wrapped rubber drain was imbedded in the wall of the aneurysm and at one point was actually lying free inside of the lumen (Fig. 9). On cut surface the polyethylene was evident about part of the aneurysmal wall (Fig. 9). The intimal surfaces were covered with atherosclerotic plaques, and over the anterolateral surface a laminated thrombus was noted. Microscopically, a slight amount of dense hyalinizing fibrous connective tissue was present in the outer portion of the anterolateral wall of the aneurysm covered by polyethylene (Fig. 10*a*). Posteriorly, the wall of the aneurysm was of the same thickness, and little difference was noted between the external surface of this area and that covered by polyethylene (Fig. 10*b*).

Case 5.—E. S., a 68-year-old white man, was first admitted to the Methodist Hospital on May 28, 1952, with a history of a pulsating mass in the upper portion of the abdomen of two years' duration. Two weeks prior to admission he experienced moderately severe abdominal pain in the region of the mass. Examination of the abdomen disclosed a firm, pulsating, nontender mass about 8 cm. in diameter to the right of the midline. Roentgenograms of the abdomen demonstrated a round soft tissue mass in the right lower quadrant with small flakes of calcium in the wall and laminated densities in the right upper quadrant, presumed to be gallstones. Results of laboratory tests were within normal limits.

On June 2, 1952, operation revealed an aneurysm of the abdominal aorta extending from the level of the inferior mesenteric artery above to the bifurcation below and measuring approximately 7 by 9 cm. (Fig. 11). The posterior peritoneum was incised, and the aneurysm was exposed on its anterior and lateral surfaces. Bilateral lumbar sympathectomy was performed. The aneurysm was covered on its exposed surfaces with a sheet of reactive polyethylene, which was sutured to the aneurysmal wall in several places. Appendectomy and cholecystectomy were then performed. Convalescence was uneventful, and on June 11, 1952, the patient was discharged from the hospital.

The patient continued to have abdominal pain at home, and on April 15, 1953, he was readmitted to the hospital, complaining of progressive increase in severity of symptoms and in size of the abdominal mass. Physical examination and roentgenograms revealed an increase in size of the abdominal aortic aneurysm. In addition, both lower extremities were moderately edematous. On April 17, abdominal exploration revealed the aneurysm to have increased significantly in size since the initial operation, about 10½ months previously, extending from a point just below the renal arteries to involve the internal iliac arteries (Fig. 12). The external iliac arteries, however, appeared to be free of aneurysmal dilatation. The cellophane with which the aneurysm had been wrapped was readily identified, and little or no reaction was demonstrable on the wall of the aneurysm or in the perianeurysmal tissues. The aneurysm was excised, and the defect was bridged with an aortic bifurcation homograft. Distally, anastomosis of the graft was made to the external iliac arteries, the internal iliac arteries being destroyed by the aneurysm. Convalescence was uneventful, and the patient has remained well since discharge from the hospital on May 5, 1953.

Fig. 12.—Photograph at operation 10½ months after the aneurysm was wrapped with polyethylene film (Case 5). The tremendous increase in size of the aneurysm, particularly in a longitudinal direction, is evident. It now extends distally to involve both internal iliac arteries. There is no evidence of reaction external to the polyethylene.

The specimen consisted of an abdominal aortic aneurysm measuring about 20 by 12 cm. On section it was partially filled with laminated thrombi, both old and recent, which occupied almost the entire anterior portion of the aneurysmal sac.

Microscopically, the inner surface of the aneurysm was lined by a thrombus with slit-like spaces and deposits of calcific granules. This was contiguous with coarse collagenous bundles that, in the outer layers, contained streaks of connective tissue

and blood vessels. Surrounding these were infiltrations of lymphocytes, plasma cells, and large mononuclear cells. In some areas extravasations of erythrocytes spread apart all the elements of the wall. On the surface adjacent to the polyethylene there was slight condensation of collagenous fibers (Fig. 13).

Case 6.—L. H., a 68-year-old white man, was admitted to the Methodist Hospital, on Aug. 19, 1952, complaining of mild mediabdominal discomfort and a pulsating mass diagnosed as an abdominal aortic aneurysm. At operation on Aug. 20, the fusiform aneurysm was found to arise well below the renal arteries and extend to approximately 2 cm. above the aortic bifurcation, measuring approximately 6 by 8 cm. A polyethylene ligature was tied about the

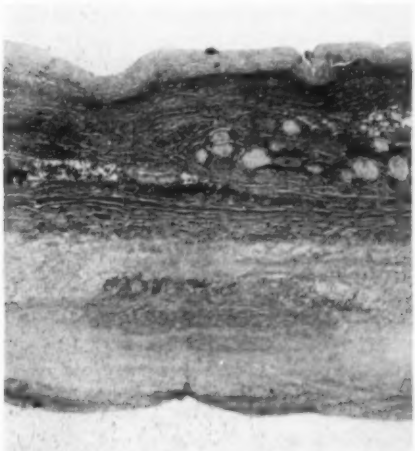


Fig. 13.—Microscopic preparations from the anterior wall of the aneurysm (Case 5) showing a thin layer of dense hyalinizing fibrous connective tissue on the surface adjacent to the polyethylene; reduced 3/10 from Mag. × 30.

aorta above the aneurysm to produce partial occlusion, and a sheet of polyethylene was placed over the aneurysm, completely encircling it in three places. After discharge from the hospital, the patient remained well for about a year and then began to experience some recurrence of abdominal discomfort and gradual increase in the mass. He was readmitted to the Methodist Hospital on June 1, 1954, because of these symptoms.

At operation on June 4, 1954, approximately 21 months after the initial procedure, the aneurysm was found to have increased in all diameters, extending from just below the renal arteries to involve the aortic bifurcation and proximal portions of both common iliac arteries. The aneurysm was resected and replaced with an aortic bifurcation homograft. Convalescence was uneventful and the patient was discharged on June 15.

Fig. 14.—Resected aneurysm of the abdominal aorta 21 months after it was wrapped with polyethylene film and the aorta just proximal to the aneurysm constricted with a polyethylene ligature (Case 6). Cut surfaces show polyethylene covering both anterior and posterior surfaces. In places the polyethylene is covered by a thin film of fibrous tissue, while elsewhere there appears to be no reaction about it. The lumen of the aneurysm is partially filled with a laminated thrombus. The polyethylene ligature has produced no alteration in the lumen of the aorta.

The aneurysm measured 10 by 13 cm. Portions of the polyethylene ligature were visible in the upper third of the wall of the aneurysm (Fig. 14). Elsewhere the polyethylene was covered by a thin membrane, which had been disrupted in places, exposing the polyethylene beneath. On section, the anterior portion of the aneurysmal sac was filled with old and recent thrombi that were laminated in places (Fig. 14). The thickness of the posterior wall of the aneurysm was equal to that of the polyethylene-

Fig. 15.—Microscopic preparation from the wall of the aneurysm (Case 6). There is a layer of dense hyalinizing fibrous connective tissue external to and beneath the space occupied by the polyethylene film; reduced 3/10 from Mag. × 30.

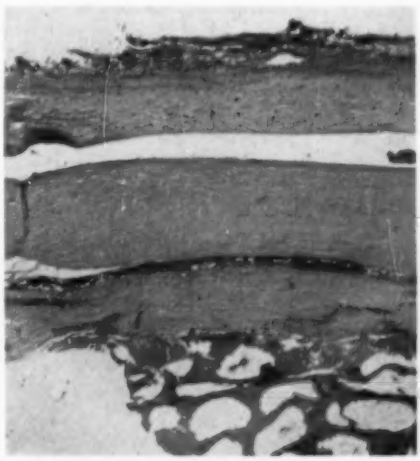


Fig. 16.—Microscopic preparation from the anterior wall of the aneurysm (Case 7). There is dense hyalinizing fibrous connective tissue above and below the space occupied by the polyethylene. There are infiltrations of lymphocytes, plasma cells, and large mononuclear cells about the vasa vasorum in the adventitia; reduced ½ from Mag. × 50.

covered anterior wall (Fig. 14). Although the polyethylene encircled the aneurysm in three places, there was no gross evidence that the wall was broadened in these areas.

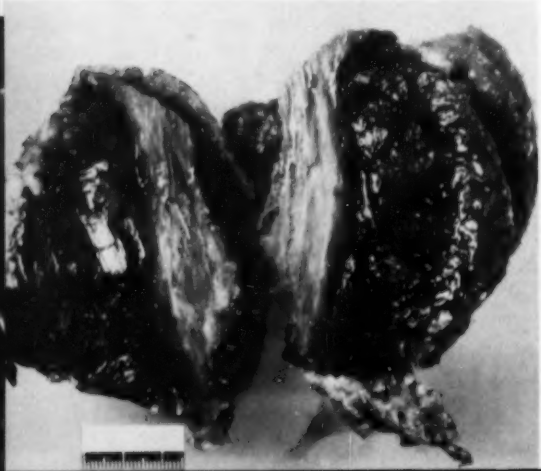
Microscopically, the thrombi were in various stages of organization. Extensive atheromatous changes had replaced almost all the wall of the aneurysm. In those areas covered with polyethylene there was a thin layer of dense hyalinizing fibrous connective tissue immediately external to, and beneath, the polyethylene (Fig. 15). In some places aggregations of lymphocytes amounted to follicle formation. In other regions beneath the cellophane there were infiltrations of lymphocytes, plasma cells, and large mononuclear cells.

Case 7.—J. M., a 46-year-old Negro man, was admitted to the Surgical Service at the Jefferson Davis Hospital on July 4, 1951, with an aneurysm of the innominate artery. Since the patient had a positive serologic reaction for syphilis, the aneurysm was presumed to be syphilitic in origin. On July 12, at thoracotomy, the aneurysm, which was found to arise from the arch of the aorta and to involve the innominate artery, was excised and lateral aortorrhaphy was carried out.[5] Physical examination disclosed, in addition to this aneurysm, a small aneurysm of the abdominal aorta. After discharge, the patient was followed in the outpatient clinic and from time to time complained of abdominal pain associated with nausea and vomiting. The pain was unrelieved by food or alkali. Several roentgenograms of the upper gastrointestinal tract failed to reveal any abnormality.

On Nov. 29, 1951, abdominal exploration disclosed a small fusiform aneurysm in the terminal aorta just proximal to the bifurcation, measuring about 5 by 7 cm. It was freed from surrounding structures and wrapped with reactive polyethylene film. No other abnormalities were noted at that time.

On Jan. 8, 1953, the patient was readmitted to the hospital because of continued abdominal pain and slight increase in the size of the abdominal aneurysm. On Jan. 12, about 13 months after the aneurysm had been wrapped, abdominal exploration was again carried out and showed the aortic aneurysm to have increased somewhat in size since that time. The cellophane was covered completely by a thin layer of fibrous connective tissue. The aneurysmal dilatation extended to the left iliac artery as far as its bifurcation. The involved segment of the aorta was resected and replaced with an aortic bifurcation homograft. The patient was discharged from the hospital on Jan. 21 in good condition, and he has remained well since then.

Fig. 17.—Resected aneurysm of the abdominal aorta seven months after it was wrapped with polyethylene (Case 8). Cut surfaces show an eccentrically placed laminated thrombus with areas of liquefaction necrosis between the thrombus and the aneurysm wall.



The specimen measured 7 by 10 cm. The proximal portion of the aorta at the beginning of the aneurysm and the common iliac arteries was thick-walled and brittle. In some areas the aneurysmal wall measured about 1 cm. in thickness, whereas in others it was less than 1 mm. A laminated grayish red and yellow thrombus occupied a portion of the aneurysmal sac and was eccentrically placed. Overlying the polyethylene was a thin layer of shaggy, membranous fibrous tissue.

Microscopically, there was pronounced hyaline change throughout the media, with some infiltration of lymphocytes in scattered areas. Around much of the media were large deposits of pink, amorphous or granular material surrounding varying-sized, numerous, cleft-like spaces. The intima was not discernible. Attached to the intimal surface was a layer of pink, fibrillar and granular debris with a laminated pattern representing the thrombus. Within the media calcification was evident. There was increase of the fibrous connective tissue in the adventitial layer. Throughout, there was infiltration of inflammatory cells. An elongated strand of homo-

geneous material which represented the polyethylene was attached to the outermost portion of the adventitial layer. Overlying this and extending from an area of the adventitia not covered by this material was a thin layer of hyalinized fibrous connective tissue (Fig. 16).

CASE 8.—V. C., a 60-year-old white patient, was first admitted to the Methodist Hospital on Aug. 4, 1952, with a history of a pulsating mass and aching abdominal pain of one month's duration. Physical examination revealed a pulsating mass in the upper part of the abdomen, and an aortogram clearly defined the fusiform aneurysm arising just below the renal arteries and extending distally to just above the bifurcation. On Aug. 7, abdominal exploration revealed a fusiform aneurysm involving

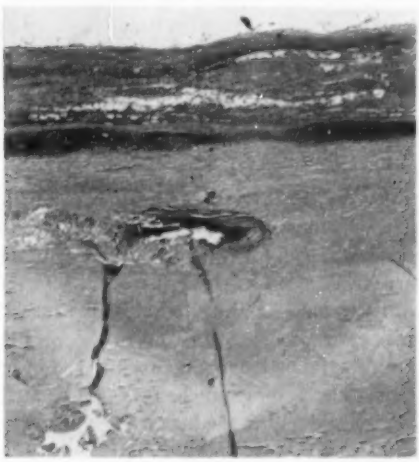


Fig. 18.—Microscopic preparation from the wall of the aneurysm (Case 8) showing a slight reaction in the adventitia consisting of a layer of dense hyalinizing fibrous connective tissue; reduced 3/10 from Mag. × 30.

the abdominal aorta arising just below the renal arteries and measuring about 6 by 8 cm. The posterior parietal peritoneum was incised and dissected from the aneurysm. Because of the dense adherence of the aneurysm to the posterior aspect of the fourth portion of the duodenum and its adherence to surrounding structures on its posterior and right lateral aspects, these areas could not be exposed. The aorta proximal to the aneurysm was dissected free, and a folded piece of polyethylene film was tied about the aorta so as to occlude the vessel partially. After placement of this polyethylene ligature, pulsations in the aneurysm were significantly reduced. A large sheet of polyethylene film was sutured over the exposed anterior and left lateral aspects of the aneurysm, and the posterior parietal peritoneum was closed over it. The postoperative course was uneventful, and the patient was discharged Aug. 16, 1952.

On March 14, 1953, he was readmitted to the hospital because of recurrent abdominal pain and increase in size of the aneurysm several months previously. Physical examination revealed enlargement of the aneurysm in both horizontal and vertical diameters and apparent prominence toward the left. At operation on March 16, about seven months after the initial procedure, the aneurysm was exposed. Its surface appeared granular, although the wall appeared to be thin. The aneurysm now arose just below the renal arteries and extended distally to include the bifurcation of the aorta. The involved segment of aorta was excised and replaced with a bifurcation homograft. Convalescence was uneventful, and the patient was discharged on March 29, and has since remained well.

The specimen measured 12 by 10 cm. and was filled with an eccentrically placed laminated clot (Fig. 17). Microscopically, there was distortion of the wall of the aorta with atherosclerotic changes in the intima which was thickened and filled with slit-like spaces. The media was greatly compressed and distorted and showed a fairly heavy infiltration of lymphocytes and plasma cells. In places the adventitia was slightly thickened owing to hyalinizing fibrous connective tissue (Fig. 18). External to the polyethylene a similar layer of fibrous connective tissue was noted. With the aid of polarized light, fragments of polyethylene were discernible in these areas, some of which were surrounded by giant cells of the foreign body type. Elsewhere the adventitia was loose, with infiltrations of lymphocytes, plasma cells, and large mononuclear cells.

COMMENT

Clinically varying degrees of symptomatic improvement occurred after the polyethylene wrapping procedure in most of these patients and in a few this lasted for about a year. In all the patients, however, there was recurrence of symptoms and progressive increase in size of the aneurysms. This enlargement in the dimensions of the aneurysm varied from slightly less than a fourth to about twice the size at the initial operation. In some this took place slowly and gradually, while in others once it began it seemed to develop rapidly.

At the second operation a characteristic finding was a relatively minimal degree of fibrosis in the tissues immediately overlying the sheets of polyethylene. Indeed, it could often be observed glistening through the thin

overlying posterior peritoneal layer. The impression was gained that the presence of the polyethylene actually facilitated mobilization of the aneurysm from the surrounding tissues.

Morphologic studies of the resected specimens revealed that the maximum response to the polyethylene consisted in formation of a thin layer of dense hyalinizing fibrous connective tissue in some areas of the aneurysmal wall in contact with the polyethylene. In other areas covered by polyethylene, however, there was no evidence of a similar tissue response to the implanted material. The polyethylene appeared to have produced no reaction whatever in one patient, and in none of them was the reaction equal to that observed in experimental animals. In fact, on the basis of these pathologic findings, it is unlikely that the reaction induced by the implanted polyethylene could have favorably altered the natural course of the aneurysms.

This lack of response to polyethylene, which has been noted by others, has been attributed to improper methods of sterilization or to the use of polyethylene containing too little of the reactive agent, dicetyl phosphate.¶ In all patients herein reported, Du Pont Polythene N. V. 7-14, containing slightly less than 1% dicetyl phosphate, was used. This type of material has been employed both experimentally and clinically with apparently satisfactory results.# In addition, Berman [2] reported that a solution of less than 1% dicetyl phosphate, when injected intramurally, produces a pronounced fibroblastic response in the wall of aneurysms. The Polythene was sterilized by immersion in aqueous cetylpyridinium chloride for 30 minutes, a method which has been reported to have little effect on the reactive agent, dicetyl phosphate.[27] It appears that polyethylene film containing dicetyl phosphate induces a fibrous connective tissue reaction in the adjacent wall of an aneurysm, but this reaction is not severe enough to be clinically effective.

¶ References 7 and 27.

References 28 and 34.

In each instance, a laminated clot adherent to the inner surface of the anterior wall of the aneurysm increased the thickness of the wall to several centimeters in places. The posterior wall, however, was frequently thin and friable and had undergone extensive atherosclerotic change. It was not technically feasible to apply polyethylene to the entire posterior wall, because of the lumbar arteries, or in some instances to the right posterolateral wall, because of adherence to the inferior vena cava. Thus, in the portions of the aneurysms over which polyethylene could be placed in some of the cases the wall was already strengthened by organized thrombus, and the fibrous connective tissue reaction resulting from the polyethylene film was not induced in areas where it was needed most.

As emphasized previously,[6] the polyethylene wrapping procedure may have an unfavorable effect by its potential tendency to devitalize the sac. Application of an impervious material to the surface of the aneurysm, by separating the aneurysm from surrounding tissues, may seriously interfere with the blood supply to its wall. In fact, areas of necrosis were noted in the wall beneath the polyethylene in two resected specimens. The pathologic changes that occur in the wall and within the lumen of an aneurysm predispose to weakening and rupture. Loss of elastic fibers and replacement of intima and media by atherosclerotic lesions are characteristic of the arteriosclerotic aortic aneurysm. Laminated thrombi, formed within the lumen, undergo organization in some areas and liquefaction in others. Characteristically, this liquefaction necrosis is interposed between the aneurysmal wall and the partially organized thrombus (Fig. 17). Under these circumstances, the blood supply of the aneurysmal wall is derived entirely from periaortic tissues. Reported instances of rupture of aortic aneurysms following wrapping with polyethylene have probably resulted in some cases from extensive separation of the aneurysm from surrounding structures, with consequent disruption of the major portion of the blood supply to its wall and implantation of an impervious material

between the aneurysmal wall and the periaortic tissues, preventing development of a new blood supply. It appears, therefore, that the treatment of aortic aneurysms by wrapping with reactive polyethylene not only fails to promote effectively thrombosis within the aneurysm and reinforce significantly the wall by stimulation of fibrous connective tissue but may, in fact, be contraindicated.

Resection of the aneurysm with restoration of continuity by lateral aortorrhaphy or replacement by homograft is now considered the procedure of choice and may be employed in most cases.[10] With the rapidly accumulating experience demonstrating the efficacy of this method of treatment, the need for a procedure such as polyethylene wrapping, which at best is only palliative, is fast diminishing. Perhaps in the few cases in which removal of the aneurysm is not feasible, the purpose of this form of therapy may be better attained by application of a fibrogenic agent, such as dicetyl phosphate, in the form of an injectable suspension.[2]

SUMMARY

Previous reports based upon certain experimental studies and clinical observations have suggested that the polyethylene wrapping procedure, with use of polyethylene film containing dicetyl phosphate to produce a fibroblastic response, may be useful in the treatment of aortic aneurysms. Its efficacy, however, clinically has not been well established.

Eight cases of aneurysms of the abdominal aorta previously treated by polyethylene wrapping and subsequently resected are reported. The interval between the cellophane wrapping procedure and subsequent resection varied from 7 to 41 months.

Although symptomatic improvement following the polyethylene wrapping procedure occurred in some of the patients, there was recurrence of symptoms and progressive increase in size of the aneurysms in all the patients.

Morphologic studies demonstrated that the fibroblastic reaction was both grossly and histologically inadequate to provide significant reinforcement. The conclusion is reached that it is unlikely that the reaction induced by the implanted polyethylene could have favorably altered the natural course of the aneurysm.

There is reason to believe that the polyethylene wrapping procedure may have an unfavorable effect by its potential tendency to devitalize the sac.

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EXPERIMENTAL SURGICAL APPROACH TO AORTIC VALVE

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SURGEONS have not yet developed a safe approach to the aortic valve. Previous attempts have been reported by Bailey and co-workers,* Brock,[3] and Niedner.[7] Bailey and others,[2] in an excellent review of the subject of aortic stenosis, gives a full account of the methods used to date in reaching the aortic valve by himself and others.

Both the ventricular and the aortic routes are hazardous because of conditions peculiar to the tissues traversed. With surgical trauma the ventricle tends to fibrillate; in aortic stenosis the intraventricular pressures are extremely high, and the hypertrophied myocardium may be unable to hold closing sutures. The proximal aortic wall has poor strength and elasticity. It will bleed alarmingly from fine needle holes, will tear easily rather than stretch, and may fail to hold sutures placed for hemostatis during ventricular entry. After due study we chose to develop the aortic approach. In our first series of experiments, numerous procedures were performed on 70 dogs. These can be roughly arranged as follows:

1. Direct aortotomy of unobstructed aorta
2. Aortotomy through tunnels of approach
   (*a*) vein
   (*b*) rubber
   (*c*) auricular appendage
3. Aortotomy through aortic reinforcement by
   (*a*) fibrosing plastics alone
   (*b*) free autografts of amputated appendage
      1. without fibrosogenic plastics
      2. with fibrosogenic plastics
   (*c*) homografts of auricular appendage
   (*d*) dicetyl phosphate on oxidized cellulose (Oxycel)

Our greatest initial success was obtained by reinforcing the denuded proximal aortic wall with free fresh autografts and preserved homografts of amputated auricular appendage. The thickness of the aortic wall was thus increased to as much as 1 cm. Through

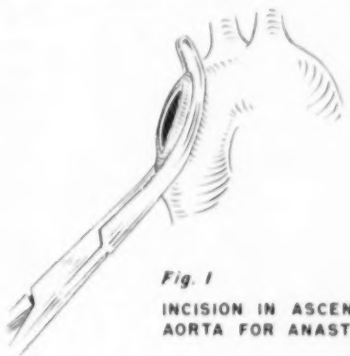

Fig. 1

INCISION IN ASCENDING AORTA FOR ANASTOMOSIS

a purse-string suture in such a reinforced area, at a second operation 7 to 15 days later, we were regularly able to enter the left ventricle through the aortic valve, with complete control of hemorrhage and with survival of the animal.

However, when we killed dogs from two to three and one-half months after this procedure and examined the area of aortic entry, we were disappointed to find that (1) the intimal surface of the aorta did not heal, and that (2) small aneurysmal pockets lined with very small clots appeared between the aortic wall and the graft in a moderate number of specimens. The second stage was almost always extremely difficult because of the dense adhesions between aorta, graft, pericardium, and lung, the freeing of which too often resulted in serious injury to the

This project has been supported by grants from the San Francisco Heart Association and from the Louis Brounstone Memorial Fund.

Presented at the meeting of the North American Chapter of The International Society of Angiology, San Francisco, June 19, 1954.

From the Harold Brunn Institute of Cardiovascular Research and the Department of Sympathetic and Vascular Surgery, Mount Zion Hospital.

* References 1 and 2.

lung. We therefore decided that the approach to the aortic valve and left ventricle through an area of aorta thus reinforced was not entirely satisfactory and sought a method whereby the aortic valve could be approached safely in one stage and the aortic wound could be deliberately approximated for healing per primam intentionem.

PROCEDURE

A second technique was therefore developed as follows: With the dog on his right side the chest is opened through the third left intercostal space. The phrenic and vagus nerve are freed and retracted posteriorly. The upper portion of the pericardium is opened to the aortic attachment, and the

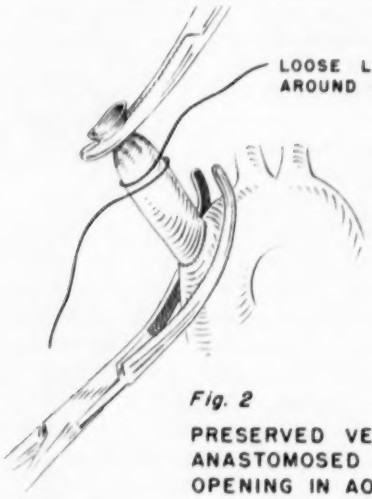

Fig. 2

PRESERVED VEIN GRAFT
ANASTOMOSED TO
OPENING IN AORTA

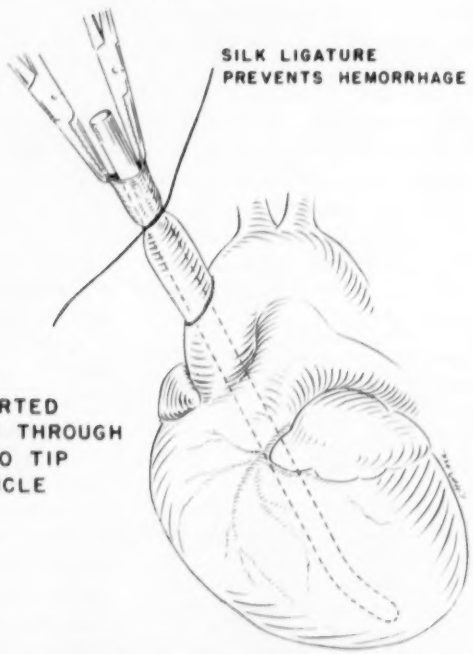

Fig. 3

GLASS ROD INSERTED
INTO GRAFT AND THROUGH
AORTIC VALVE TO TIP
OF LEFT VENTRICLE

ascending aorta denuded. A segment of ascending aorta is then pinched off by means of a curved Glover clamp so as to permit a good flow through the aorta (Fig. 1). A graft of vein preserved at 0 C. for from 1 to 42 days is then anastomosed to the aorta by a leak-proof technique which stands the high aortic pressure (Fig. 2). A finger or curved glass rod, depending on the size of the aorta, is inserted into the open end of the graft. the latter withdrawn. The curved clamp is reapplied to the aorta and the graft transected about 0.5 cm. from the anastomosis (Fig. 4). The anastomosis is then disconnected by cutting and removing all the sutures, and the remainder of the graft is removed (Fig. 5). The aorta is closed by one layer of interrupted mattress sutures reinforced by a simple over-and-over running suture of 00000 nonabsorbable (surgical) silk and the clamp

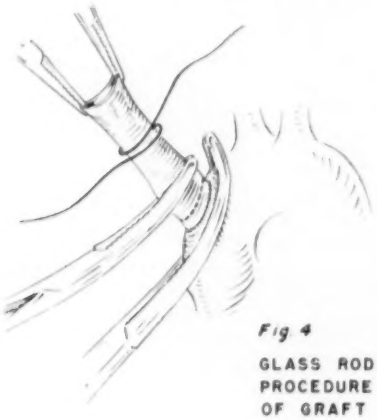

Fig. 4

GLASS ROD WITHDRAWN; PROCEDURE FOR REMOVAL OF GRAFT

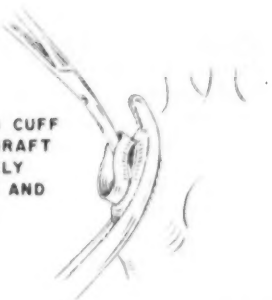

Fig. 5

REMAINING CUFF OF VEIN GRAFT COMPLETELY DETACHED AND REMOVED

Fig. 6

CLOSURE OF AORTIC OPENING IN TWO LAYERS

Most dog aortas are too small to accommodate the finger so that the rod is usually employed. A ligature of heavy silk is placed around graft and the enclosed rod and held just tightly enough to control bleeding. As the clamp on the aorta is removed, the rod is inserted through the aortic valve to the tip of the left ventricle (Fig. 3). The heart reacts little or not at all to the presence of the foreign body. The rod is withdrawn from the aorta into the graft so that its tip is between the anastomosis and the ligature. The graft is clamped proximal to the rod and removed (Fig. 6). The aortic wound is further reinforced by a piece of oxidized cellulose (Oxycel), and the periaortic fat approximated snugly over the suture line.

Thus the preserved vein segments are used only as temporary prostheses to permit safe ventricular entry. Since no part of the vein graft is allowed to remain, it is not necessary to select veins which are compatible with the host; they need only be sterile. We have used dog homografts and human heterografts, with equal success. Vein tissue stands the aortic pressure with ease, holds sutures

well, and can be repeatedly clamped without disruption. We are investigating the replacement of veins by synthetic materials.

The new technique has been carried out in 32 dogs. Eight are living and well; six were killed. Seven died from the crushing action of an unsatisfactory aortic clamp. We have since learned to use this clamp without injuring the aorta, but a new and safer clamp is being devised. Seven died of disruption of the suture line. This has been overcome by changes in the technique of closure. One died of anesthetic shock, one from hemorrhage during denuding of the aorta, one of progressive brain damage resulting from failure of the oxygen supply, and one from rupture of an aorta damaged in a previous operation. The last six dogs survived and were killed from 2 to 4 months after operation. Autopsy showed the aortic wall at the site of entry firmly healed and the intima fully endothelialized.

Our experiments show that the aortic valve and the cavity of the left ventricle can be reached with little risk through a temporary tunnel of vein graft anastomosed to the ascending aorta. The graft permits one to control hemorrhage in the unobstructed aorta during passage of finger or instrument through the aortic valves and to withdraw them with safety. The procedure is done in one stage. Preserved vein homografts or human heterografts are equally effective as temporary prostheses. The grafts are completely removed at the completion of the intracardiac portion of the operation, and the aortic opening is closed and reinforced. The use of other substances to replace veins is under study. These experiments suggest that the previously described technique could be applied to the treatment of certain conditions of the aortic valve in man.

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INTRACARDIAC SURGERY BY LEFT VENTRICULAR BY-PASSING WITH GEMEINHARDT PUMP

WILLIAM L. JAMISON, M.D.; WILLIAM GEMEINHARDT; JAHANGIR ALAI, M.D.; ANN COIA, R.N., and C. P. BAILEY, M.D., Philadelphia

MAJOR VASCULAR surgery in which the heart is not directly attacked can be performed with a minimum of operative risk. In our opinion the reason for this is that the heart is capable of maintaining its full function throughout the period of surgical manipulation.

Performance of closed direct intracardiac surgery for such congenital conditions as pulmonic stenosis and atrial septal defect and for such acquired lesions can be accomplished with a low operative mortality, although the heart is forced to maintain its circulatory function both during and after the definitive surgery. However, it will be noted that each of these conditions is deleterious to the heart primarily because of overwork and strain of the right ventricle. Functionally, each of these conditions is a "right-sided" cardiac lesion. In each the left ventricle is spared by the disease, "protected" against overwork by the lesion itself. In fact, the left ventricle actually may seem to be somewhat "atrophic" because of underwork, although this can never be extreme, since the very maintenance of existence implies that it must produce a minimally effective cardiac output.

Today, with the natural advances in cardiac surgical thinking and method, we have begun to attack surgically certain cardiac lesions whose effect is specifically upon the left ventricle. These "left-sided" lesions, notably mitral insufficiency, aortic stenosis, and aortic insufficiency cause overwork and, eventually, exhaustion of the left ventricle, the cardiac chamber which is primarily responsible for the maintenance of the cardiac output and, hence, for the maintenance of life itself.

It is not surprising that the definitive intracardiac instrumental or digital manipulations required in the treatment of left-sided cardiac lesions momentarily should so depress the left ventricular output as frequently to precipitate an immediate acute circulatory failure. Whether this takes the form of ventricular fibrillation or of hypotension and cardiac standstill, the end-result is usually the same. Hence, it gradually became evident to us that simple intracardiac intervention for the alleviation of these left-sided lesions must inevitably be associated with an unacceptable high operative mortality.

Since recovery and improvement was the rule in those patients who survived the immediate operative insult, the thought inevitably arose of performing these operations with the aid of an extra corporeal circulation to by-pass the heart and lungs.

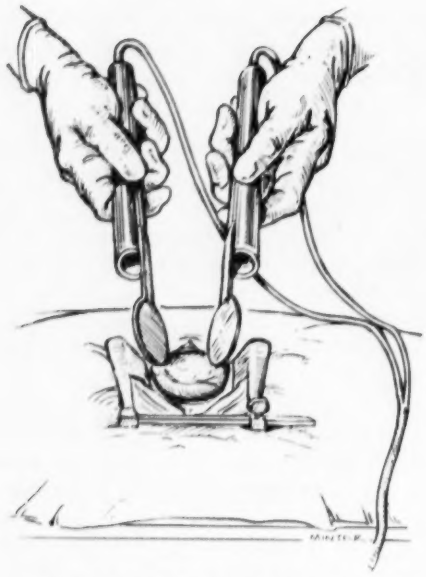
During the last 14 years, we have been concerned with the development of an extracorporeal circulation in association with an oxygenator in order to by-pass the heart and lungs completely. Today, we do not feel that any of the existing oxygenators is completely satisfactory and have come to believe that a total by-pass of the heart and lungs is in certain respects less desirable than a partial or complete by-pass merely of the left side of the heart.

These disadvantages of the total by-pass method include the reported difficulty in obtaining a good venous return when the right atrial pressure is lowered by mechanical aspiration of its contents. Furthermore, since

This work was supported by The Mary Bailey Foundation for Heart and Great Vessel Research.

Presented at the meeting of the North American Chapter of The International Society of Angiology, San Francisco, June 19, 1954.

From the Department of Thoracic Surgery, Hahnemann Medical College and Hospital (Dr. Jamison, Instructor; Dr. Alai, Fellow; Miss Goia, Research Nurse, and Dr. Bailey, Professor and Head), and The Bailey Thoracic Clinic (Mr. Gemeinhardt, Research Engineer).



1. Ventricular fibrillation is induced by holding the electrodes parallel and at right angles to the surface of the heart.

we do not contemplate direct intervention into the cardiac chambers by an open surgical technique, we see no need for a complete by-pass of any portion of the heart. We merely wish to ensure that during the period of maximal interference with the specific function of the left ventricle, sufficient oxygenated blood will be delivered into the aorta to maintain an adequate blood pressure and hence adequate perfusion of the coronary and other systemic arteries.

During the past two years, the Gemeinhardt pump has been perfected to the point where it is completely capable of by-passing the left ventricle, withdrawing blood from the left atrium and administering it retrograde fashion through the subclavian artery. Experimentally, we have found that with the pump in this position the heart can be thrown into ventricular fibrillation while an adequate level of pressure is maintained mechanically by the pump. Figure 1 shows the method of experimental induction of ventricular fibrillation by holding the electrodes parallel with and perpendicular to the heart. Figure 2 shows the application of the electrodes for defibrillation. The nurse plugs the cord into the socket and instantly withdraws it when the command "hit" is given. This method has been dependable and safe in our hands. Even rubber gloves are not worn occasionally.

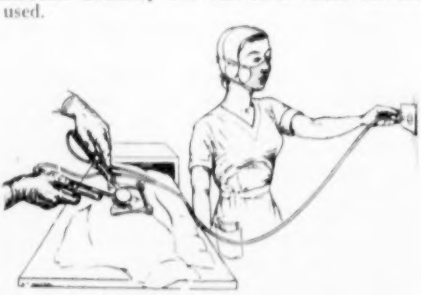
In other words, the pump, by maintaining the systemic aterial pressure, forces blood through the arterial circulation, capillaries, venous system, right heart, and lungs, and back into the left auricle. In terms of physiology, we have interpreted this to mean that the right ventricle is not necessary if the *vis-a-tergo* of the left ventricle is sufficient. This work has been reported. Experimentally, we have been able to maintain the dog's heart interventricular fibrillation with the aid of the pump for periods up to 60 minutes, with complete recovery.

With this experimental background, we felt justified in applying the pump in human surgery in the following conditions.

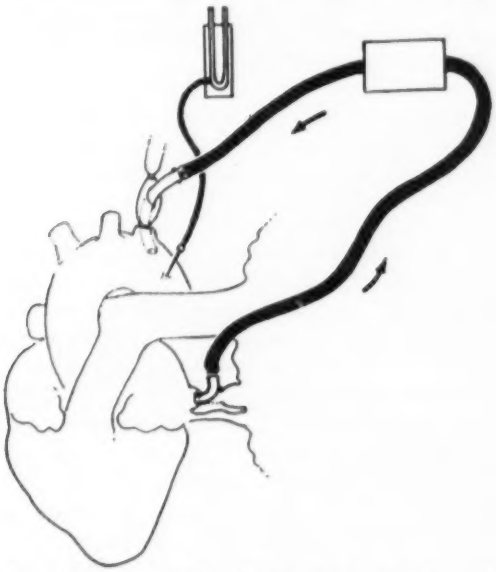
Patients with mitral stenosis, mitral insufficiency, and aortic stenosis often have a low cardiac output, which results in low blood pressure on the operating table. With the use of the Gemeinhardt pump, we have been able to raise the blood pressure and perform surgery on patients who otherwise could not be operated on. In most instances it is not necessary that the entire left atrial content be propelled by the pump.

Figure 3 shows the cannulation used in human surgery. Blood is withdrawn from the left atrium by insertion of a cannula through the left superior pulmonary vein.

2.—Defibrillation by holding the heart between electrodes. Ordinary 110 volt A.C. house current is used.



The peripheral portion of the vein is temporarily clamped off. Blood is thus withdrawn in retrograde fashion. Cannulation is performed through the left superior pulmonary vein rather than the auricular appendage, in order to leave the appendage free for the actual surgical manipulation. After passage through the pump, the blood is reintroduced into the left subclavian artery, in retrograde fashion. The subclavian artery is ligated inferior to the internal mammary artery. We have had no difficulty with circulation of the arm and the hand if the internal mammary artery is not ligated.



3.—Cannulation is performed by withdrawing blood retrograde from the left superior pulmonary vein and reintroducing it retrograde through the left subclavian artery.

In mitral stenosis, the damming-up of blood in the left auricle by the stenosed valve can be relieved by the pump so that more methodical and more accurate opening of the valve can be performed.

Figure 4 is the blood pressure curve plotted against minutes of anesthesia of a patient with mitral stenosis. Hypotension began when methoxamine (Vasoxyl) was given, with a transitory rise in blood pressure. The blood pressure fell to its former low level over 15 minutes and then rose with a second dose of methoxamine. Cannulation was then performed, and a satisfactory blood pressure was obtained when the pump was started. After the mitral valve was opened, a slight increase in blood pressure occurred. An operation on this particular patient had been cancelled once previously after severe hypotension occurred with induction of anesthesia.

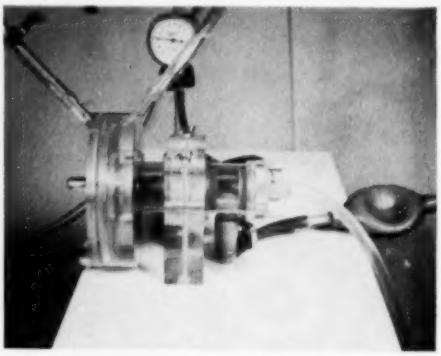
In classic cases of mitral insufficiency, the left auricular pressure is extremely high, and at times the pressure has been so high that the left auricle could not be successfully closed after simple exploration. By relieving the high pressure, adequate hemostasis for the necessary manipulations can be secured so that successful suturing of the valve can be performed.

Aortic stenosis is associated with a low cardiac output and a state of relative coronary insufficiency. The pump can maintain the coronary pressure while the aortic dilation is carried out.

The indications for the use of the pump in aortic insufficiency are not clear-cut at present, since the incompetent valve may permit blood to accummulate in the left ventricle. With the cannulation set-up previously described, experimentally we have been able

to clamp the ascending aorta for 45 minutes, with complete recovery. Clamping the ascending aorta would prevent regurgitant blood from accumulating in the left ventricle. At the same time, sufficient blood would transverse the ventricle unless the pumping action were made maximal to enter the coronary vessels and maintain the nourishment of the myocardium. At present, we believe that this indicates the proper way to handle aortic insufficiency with this type of apparatus. The fact that the ascending aortic arch can be clamped apparently with impunity opens new possibilities in the treatment of aneurysm of the ascending aorta by aterial grafting.

A brief description of the advantages of the pump follows. The low reservoir capacity of the pump (150 cc.) permits the system to be charged with saline rather than blood and thus to be kept ready for an emergency. The pump consists of three chambers—a pumping chamber, a dampening chamber to decrease the height of the pulsation,, and a combination filter and airtrap (Fig. 5). At present the minute output of our largest model is 2.5 liters. This is more than adequate to by-pass the entire left ventricular flow in dogs and in children. However, as an auxiliary support to the circulation it has proved invaluable in adults. A larger model is now in process of construction. The stroke volume can be varied from 5 to 25 cc. and the rate from 80 to 300. At present, it has been found best to maintain a rate of 100 and vary the stroke volume. Heparin is given in man in a dosage of 1.2 mg. per kilogram of body weight. This is much less than is necessary in the dog in which a dosage of 2 to 2.2 mg. per kilogram was given. Good control of the coagulation time has been obtained with protamine. Because the heparin is used up by circulation through the pump, it has been our routine to give only the required dose of protamine to neutralize the given dose of heparin (protamine is thought to neutralize heparin milligram for milligram). A coagulation time is then taken before further protamine is given.



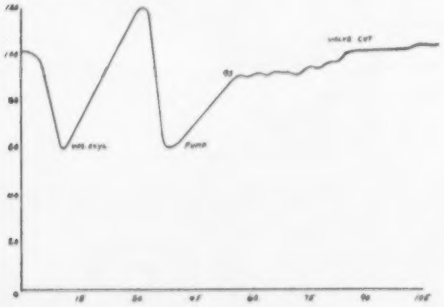
5.—Showing pumping, dampening and filter-air-trap chambers of pump.

The early models of this pump were constructed of Lucite and, therefore, could not be sterilized by autoclaving. Cold sterilization with aqueous benzalkonium (Zephiran) was used. At present, a new model is being constructed of glass and metal so that the entire unit can be autoclaved.

The low reservoir capacity does away with the necessity of using homogenous blood and thus eliminates the danger of transfusion reactions. This also decreases the necessary dosage of heparin and enables the pump to be applied without the risk of hemorrhage.

We believe that with the aid of this pump surgery can be performed in poor-risk patients that would not otherwise be possible.

4. Blood pressure plotted against minutes of anesthesia of a patient on whom hypotension was relieved by the pump.



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STUDY OF BASIC PHYSIOLOGIC CHANGES ASSOCIATED WITH HYPOTHERMIA

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THE SEARCH for a method which would permit intracardiac surgery under direct vision has focused attention on induced hypothermia by surface cooling as a means to this end. Bigelow first demonstrated that significant reduction of oxygen consumption of the tissues occurred as a result of lowering body temperature and that during profound hypothermia the circulation could be interrupted for as long as 15 minutes.* Confirmation of these observations has come from additional experiments on animals and from clinical experience with hypothermia during surgery of the heart and great vessels.† However, the relatively high incidence of ventricular fibrillation and death in dogs at body temperatures below 28 C. poses a real hazard for practical application to clinical surgery. Furthermore, little is known of acid-base balance and metabolic behavior in mammals in the hypothermic state, and the few studies which have been made are in disagreement.‡ The studies presented in this paper were designed to provide further information on the physiological effects of reduced body temperature, with particular reference to some of the alterations in acid-base balance.

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Supported by grants from the New York Heart Association, National Tuberculosis Association, and by an Eli Lilly grant.

Presented at the meeting of the North American Chapter of The International Society of Angiology, San Francisco, June 19, 1954.

* References 1, 2, and 3.

† References 4-8.

‡ References 9 and 10.

METHODS

Thirty adult mongrel dogs were subjected to a reduction in body temperature to 21 to 18 C. over a period of 45 to 90 minutes. Sodium pentobarbital (30 mg. per kilogram) was given intravenously, after which the hair was clipped from the body. The trachea was then intubated and the endotracheal tube connected to a Rand respirator delivering oxygen and supplementary inhalation anesthetic agents through a Heidbrink machine with a circle canister. Muscle relaxants (*d*-tubocurarine, decamethonium bromide, or succinylcholine) were administered when necessary to suppress marked shivering and spontaneous respiratory efforts. The dogs were wrapped in rubber sheets and packed in ice until the desired lowering of body temperature was almost achieved. In general, a further reduction in rectal temperature of 3 to 5 C. occurred after removal of the animal from the ice. At this time, warming was begun with a Thermo-Rite machine. The dog was wrapped in a rubber blanket through which hot water circulated. Since we were interested in the effects of cooling alone, no surgery was performed beyond that required for the cannulation of peripheral vessels. Rectal temperatures were taken with a mercury thermometer.

The oxygen and carbon dioxide content of whole blood and the carbon dioxide content of plasma were determined from arterial blood samples by the method of Holaday and Verosky,[11] with a Kopp-Natelson microgasometer. Oxygen capacity and hematocrit determinations were done by standard methods.

The plasma pH of arterial blood was measured in a glass electrode by the method of Holaday.[12] The electrode was maintained at 37 C. for determinations on samples drawn when the body temperature of the dog was between 37 and 28 C. The temperature of the electrode was lowered to that of room temperature for determinations made on blood obtained when the body temperature of the dog was below 28 C. The pH value thus obtained was corrected to the exact body temperature of the animal. This was achieved by subtracting the temperature of the electrode from the observed temperature of the animal, multiplying this difference by the factor —0.015,§ and adding this value to the pH reading.

§ References 13 and 14.

The values for bicarbonate, pCO_2, and concentrations of buffer base and carbonic acid were derived from determinations of carbon dioxide content, pH, hematocrit and oxygen saturation of whole blood or plasma samples. On blood samples drawn when the body temperature was in the region of 37 C., the nomogram of Singer and Hastings was used.[15] On blood samples drawn at lower temperatures, the values were calculated from the Henderson-Hasselbach equation. Corrections were made for changes in the dissociation constant, pK', and in the solubility of carbon dioxide with decreasing temperatures. The pK' increases 0.005 units per degree centigrade fall in temperature.‖ Exact data were not available for changes in the solubility of carbon dioxide in plasma for temperatures other than 38 C., although such values are known for water. It is known also that the solubility of carbon dioxide in plasma at 38 C. is 93.4% of that in water at this same temperature.[17] The solubility of carbon dioxide in plasma was thus calculated from the values for water at lower temperatures, assuming the relationship to be constant. Blood urea nitrogen, blood sugar, prothrombin time, and venous clotting time were measured by standard methods. Serum sodium and potassium levels were determined in a Beckmann flame photometer; serum chlorides by the method of Schales and Schales,[18] and lactic acid by the method of Barker and Summerson.[19] These determinations were not done on all animals. Arterial blood samples were taken from a catheter in the carotid artery and venous samples from a catheter in the right auricle.

Oxygen consumption was measured on nine animals with a bell spirometer. Artificial respiration was maintained during the measurement by alternately raising and depressing the spirometer bell manually. Direct measurements and recordings of arterial and venous pressure were made using Sanborn electromanometers and two-channeled recorder. The standard limb leads of the electrocardiogram were recorded.

The animals are divided into three groups on the basis of differences in the pattern of artificial respiration maintained. In Group I, comprising 16 animals, the respirator was set to deliver an inspiratory pressure of 12 to 15 mm. Hg at a rate of 20 per minute. This pattern was maintained by adjustments of the respirator as needed. Group II, comprising six animals, were ventilated at the same

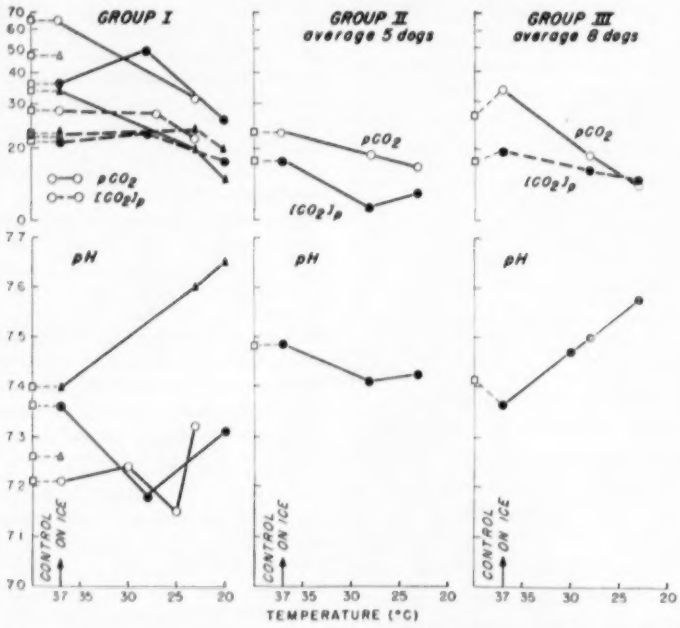

Fig. 1.—Alterations in acid-base components during hypothermia. Group I: The values for carbon dioxide content, pCO_2 and pH have been plotted for individual animals against changes in body temperature. Two of four died of ventricular fibrillation before completion of the study. Group II: An average curve has been derived for five of six animals. Group III: An average curve has been derived for the eight animals. Detailed discussion is in the text.

‖ References 13 and 16.

TABLE 1.—*Control and Recovery Acid-Base Values*

	Temp., C.	pH	pCO_2, Mm. Hg	$(CO_2)c$ mMol/L.	Buffer-Base, Eq/L.	Hematocrit, %
Group I						
Dog A	37	7.4	33.5	18.01	42.5	39.4
	37	7.15	65	20.52	40	50
Dog B	37	7.36	36	18.4	41.5	32.9
	37	....	....	12.2	....	31.8
Dog C	37	7.36	47	19.27	40	35.9
	Ventricular fibrillation at 23 C.					
Dog D	37	7.21	66	24.48	44.1	37.2
	Ventricular fibrillation at 20 C.					
Group II						
Dog E	37	7.52	19.5	13.5	41.0	35.9
	37	6.98	45.9	9.7	23.7	27.0
Dog F	37	7.48	35.2	17.7	45	47
	Ventricular fibrillation at 20 C.					
Dog G	37	7.41	28.5	15.3	42.5	41.8
	37	7.25	33.41	13.86	37	42.1
Dog H	37	7.396	29.8	15.4	41	36.7
	28	7.63	8.976	9.5	....	45.8
	37	7.255	32	12.5	35.8	43.9
Dog I	37	7.363	25.0	10.3	41	36.7
	37	7.178	22.9	6.7	28	45.8
Dog J	37	7.66	16.1	12.5	46.5	41.8
	37	....	....	8.2	....	42.3

pressure as Group I but at a rate of 25 to 30 per minute. In Group III, consisting of eight dogs, the rate and pressure of respiration was adjusted so as to obtain a plasma pH of 7.4 or above before cooling was begun. This usually required a pressure of 8 to 12 mm. Hg and a rate of 16 times per minute. Frequent determinations of plasma pH were made throughout the cooling period, and the inspiratory pressure was increased whenever the pH tended to fall. The animals in this last group were killed at the lowest temperature reached.

RESULTS

The changes in components of acid-base balance differed in these three groups of animals. The plasma carbon dioxide content, pCO_2, and plasma pH during cooling have been plotted against temperature for each of the three groups in Figure 1. The values obtained at 37 C. before cooling was begun and after warming for both the respiratory and metabolic components of acid-base balance are listed in Table 1. Hematocrit values are presented in Table 2.

Acid-base studies were done in only four dogs in Group I. Since there was a great degree of variability in the results obtained, the values have been plotted for the individual animals (Fig. 1, Group I). Two of these dogs were acidotic at 37 C., with a high pCO_2 and normal buffer base in one and a normal pCO_2 and low buffer base in the other. The change in pH in the first animal during cooling was variable, but at 23 C. the degree of acidosis was less, as indicated by an increased pH and the low pCO_2. Ventricular fibrillation occurred in both animals at or below 23 C.—in the latter before a second sample was drawn.

In the two animals which survived, the pH values at 37 C. were normal and both buffer base and pCO_2 were slightly below normal. During cooling in one animal the pCO_2 was higher at 28 C., with a corresponding fall in pH, but at 20 C. a fall in pCO_2 to below the control value was accompanied by a lesser rise in pH. In the other dog, there was a consistent fall in pCO_2 and a consistent rise in pH. After warming, a severe acidosis was present in this latter animal, with a high pCO_2 and a low buffer base.

In Group II, the direction of the observed changes in five of the six animals studied was the same, although the magnitude of change varied. The mean of these five animals is presented in Figure 1, Group II. The

TABLE 2.—*Hematocrit Changes with Temperature*

	Hematocrit Change,* %			
	37 C.	28 C.	23 C.	20 C.
Group I				
Dog A	39.4	....	54.1	....
Dog B	32.9	....	33	....
Dog C	35.9	....	....	....
Dog K †	57	....	58	....
Dog D	37.2	....	51.6	....
Dog I	32.5	35.2	36.4	....
Group II				
Dog E	35.9	41.4	29.5	....
Dog F	47	....	....	51.8
Dog G	41.8	....	52.3	....
Dog H	36.7	....	45.8	....
Dog I	49.3	43.6	....	....
Dog J	41.8	49.2	46.8	....
Group III				
Dog M	46.7	47.9	45.1	51.8
Dog N	39.5	43.8	46.3	....
Dog O	36.3	47.7	49.7	....
Dog P	41.4	....	55.3	....
Dog Q	50.2	52.3	53.2	....
Dog R	46.7	50.6	56.2	....
Dog S	47	....	52.5	....
Dog T	40.6	51.9	52.5	....

* Hematocrit values were not always obtained when carbon dioxide and pH measurements were made.
† pH was not measured on this animal.

control pCO_2 was low in all animals. In two, the buffer base was normal and the pH was higher than normal. In the other three the buffer base values were low and the pH was normal or slightly elevated. The pCO_2 decreased with decreasing temperature. The pH fell in four animals, although not below normal, and remained unchanged in one. In the sixth animal, pH was normal; the pCO_2 and buffer base were slightly below normal. A greater percentage decrease in pCO_2, however, was accompanied by an increase in pH to 7.63. The actual values at 23 C. in this animal are included in Table 1.

Ventricular fibrillation occurred in one animal in this group, without any obvious difference in acid-base changes from the rest of the group. After warming, the surviving dogs on which pH was measured were acidotic. The buffer-base values were greatly diminished in all instances, and the pCO_2 was normal or low.

In Group III, the results are also presented in the form of a mean curve, since all changes were in the same direction (Fig. 1, Group III). The status of acid-base balance at the control temperature in this group was the same as in the Group II, i. e., low buffer base, low pCO_2, and normal or slightly elevated pH. Immediately after the application of ice there was a rise in pCO_2 and a fall in pH and a variable change in carbon dioxide content and buffer base. Between 37 and 30 to 28 C. it was found necessary to increase the positive pressure on the respirator and control shivering and spontaneous respiratory efforts by repeated injections of a relaxant drug to prevent a fall in pH. As shivering was controlled and ventilation maintained, a progressive decrease in pCO_2 and rise in pH occurred. The percentage over-all decrease in pCO_2 was greater in this group than in Group II, and the decrease in plasma carbon dioxide content was less.

Ventricular fibrillation did not occur, although body temperature was reduced to between 20 and 22 C. These animals were killed at the low temperature.

Whole blood oxygen content, oxygen capacity, and saturations were increased in animals of all groups at the lower temperatures. Oxygen saturation invariably exceeded 95%. The hematocrit value alterations showed variation, but in general there was an increase at lower temperatures (Table 2). In some instances readjustment to control values had not yet occurred in the early post-warming period (Table 1).

TABLE 3.—*Serum Electrolyte, Venous Clotting Time, and Lactic Acid Changes with Temperature*

	37 C.	28 C.	23 C.	37 C.
Serum Na, mEq./L.				
Dog G	150.6	....	148.9	154.4
Dog H	142.4	....	135.3	130.0
Dog J	147.3	....	151.4	150.6
Dog T *	158.9	....	152.3	.....
Dog U *	.....	....	142.5	143.8
Dog V *	145	....	136.3	137.5
Serum K, mEq./L.				
Dog G	3.09	....	2.66	2.73
Dog H	3.37	....	4.37	2.42
Dog J	3.09	....	3.09	2.80
Dog T	3.2	....	3.5	.....
Dog U	.....	....	2.8	2.8
Dog V	4.2	....	2.9	4.08
Serum Cl, mEq./L.				
Dog G	110.4	....	113.0	115.0
Dog H	111.7	....	110.5	102.0
Dog J	119.2	....	117.1	104.9
Venous Clotting Time, min.				
Dog T	4	....	.....	.....
Dog U	6.5	....	13	8
Dog V	6	....	17	5
Dog W	5	....	14	.....
Lactic Acid, mM./L.				
Dog E	1.39	....	.....	.....
Dog F	1.5	0.99	1.44	.....
Dog G	0.4	....	0.7	0.8
Dog H	1.0	....	0.7	0.9
Dog I	1.2	1.3	.....	2.4

* No acid-base studies were done on these dogs.

Determinations of serum electrolytes in a small number of animals revealed little if any significant deviation from normal values, and such variations as were observed were inconsistent (Table 3). A prolongation in venous clotting time was noted at 23 C., which amounted to two to three times the control value (Table 3). A recovery to normal appeared to occur with warming. No changes in prothrombin time were observed. Blood urea nitrogen and blood sugar determinations showed no significant deviations during hypothermia. Similarly, the values for lac-

tic acid in the blood of six animals during cooling and warming demonstrated no important changes (Table 3).

The response in arterial systolic pressure (9 dogs), pulse rate (16 dogs), and oxygen consumption (9 dogs) showed a consistent pattern (Fig. 2). A rise in blood pressure and pulse rate occurred in all animals immediately after the application of ice. After this there was a progressive fall in blood pressure and slowing of heart rate as the temperature fell. The degree of hypotension and the rate at which it developed varied in different animals. Below 28 C. the pulse rate at each temperature was very consistent in all animals, except in those in which ventricular fibrillation developed. In these animals the pulse rate just before fibrillation was lower than the average. Oxygen consumption fell in direct relation to temperature, and at 23 C. it approximated 25% of the control value. The rate of increase of blood pressure, pulse rate, and oxygen consumption with warming was approximately the same as the rate of fall with cooling. No changes were observed in venous pressure. The electrocardiograms indicated that the arrhythmia most commonly observed was premature ventricular contraction. Auriculoventricular block was also seen. Arrhythmias usually occurred below 24 C. and never were observed above 28 C. Ventricular fibrillation was preceded by the occurrence of multiple premature ventricular contractions in all instances. Ventricular fibrillation occurred in 6 of the 16 dogs in Group I, in 1 of the 6 dogs in Group II, and in none of the dogs in Group III. With one exception, fibrillation always occurred below 23 C. In this instance, it occurred during a period of hypoventilation at 35 C. during warming.

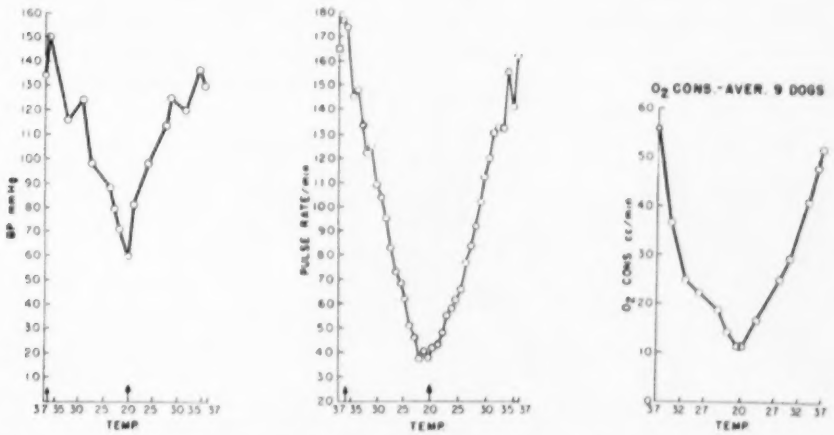

Fig. 2.—Alterations in arterial blood pressure, pulse rate, and oxygen consumption during cooling and warming. The arrow at 37 C. indicates the application of ice to the animal. The arrow at 20 C. indicates the lowest rectal temperature of these animals.

COMMENT

The results of these studies of ventilation and acid-base balance in dogs indicate that a metabolic acidosis may develop during hypothermia, as was noted by Dill and Forbes during moderate hypothermia in humans.[9] Although there is no method of quantitating the metabolic components of acid-base balance (i. e., buffer base) at lower temperatures, the development of the acidosis can be traced by inference.

In vitro, it has been found that changing the temperature of blood does not change pH if the pCO_2 is kept constant and the carbon dioxide content increases in accord with the increased solubility of the gas at lower temperatures. Conversely, if the carbon dioxide content is kept constant and the

pCO_2 decreases in accordance with increasing solubility, the pH is increased.[20]

In all dogs in this study, both the pCO_2 and the carbon dioxide content were decreased, owing to hyperventilation and decreasing carbon dioxide production. If there were no change in fixed base or fixed acid, this should result in a proportional increase in pH. Furthermore, lowering temperature diminishes the dissociation of carbonic acid and the protein buffer ions of the blood—principally hemoglobin—and thus reduces the amount of base bound by a given amount of these substances at any given pH. This factor, if the total concentration of buffers were unchanged, should also have resulted in an increase in pH. In those animals which showed a reduction of pH, the protein buffers did not remain entirely constant, since the hematocrit value exhibited either a decrease or insignificant increase. Since the total amount of buffer anion in these animals was diminished by reductions in content and by the effect of lowered temperature on the dissociation of the buffer ions and since the tension of carbon dioxide was also reduced, the obvious decreases in pH must have been derived from an increase in the fixed acids of the blood relative to the fixed base.

The samples taken in Groups I and II after warming clearly demonstrate that a metabolic acidosis did develop during the hypothermic period. However, until one can calculate the buffer base of blood at temperatures other than 37 C., the presence or absence of a metabolic acidosis in the presence of a rising pH, as seen in Group III, cannot be determined.

It has been shown that the pH decreases during hypothermia when the pCO_2 is increased owing to hypoventilation and that the pH increases when there is sufficient ventilation to cause a fall in pCO_2.[10] Swan and his co-workers[23] found a significant decrease in ventricular fibrillation in dogs which were hyperventilated as compared to a group subjected to hypoventilation.

Our observed changes in arterial pressure, pulse rate, and oxygen consumption agree with those of other observers.¶ The fact that no change was observed in venous pressure is in disagreement with an early report of Bigelow.[2] Our results are probably due to the effect of a positive-pressure respirator, which is known to decrease central venous pressure. Bigelow # has observed no significant changes in his later experiments during which there was an improved control of ventilation during cooling.

The mechanism of the increased venous clotting time is not clear, but it could have significance in the clinical application of hypothermia for cardiovascular surgery. However, there have been no reports of any significantly increased bleeding during operations performed under hypothermia. The increased clotting time may well be compensated by the slowed peripheral circulation.

Although our total number of determinations of blood electrolytes and blood chemistry studies was small, a sampling was made in the various groups in order to see if any marked deviations or inconsistencies would be revealed. In none of these studies was there found any consistent abnormality of a magnitude to be considered of real importance. Swan and his co-workers[22] have suggested a correlation of CO_2 content (pH) and serum K ion concentration which may be of importance in the mechanism of ventricular fibrillation. Although our shifts in K ion might be considered large on a percentage basis, the actual variations were within normal values. However, we would agree that the blood pH changes may be of importance, since we never observed ventricular fibrillation in dogs in which the pH was consistently increased. This suggests that factors which influence the pH, among which is ventilation, may be vital in regard to the understanding of the mechanism of ventricular fibrillation at low body temperatures.

The high incidence of ventricular fibrillation and other arrhythmias at temperatures

¶ References 1-3 and 23-25.

Bigelow, W. G.: Personal communication to the authors.

below 28 C. has been noted by many investigators. This observation would tend to support the conclusion of Hoff and Stansfield [26] that cold itself increases the susceptibility of the ventricles to fibrillation.

Additional factors suggested by others have been cardiac manipulation and air embolism in the coronary vessels. These did not play a role in our series, since no intrathoracic surgery was performed. It should be noted that the experiments reported by most investigators of hypothermia have included temporary occlusion of the cardiac inflow or even total cessation of circulation as well as some type of cardiac surgical technique. This has made most difficult a critical evaluation of the factors related to hypothermia which are capable of producing ventricular fibrillation.

It has been observed also that when the cavae are opened after temporary occlusion under hypothermia the reestablishment of blood flow in the heart is at times attended by ventricular fibrillation.* One theory suggested that an increase in epinephrine (Adrenalin) content of the static blood in the occluded inferior vena cava was sufficient to produce ventricular fibrillation when this blood entered the heart.[7] Support for the theory came from the observation that less fibrillation occurred in dogs given piperoxan (Benodaine) as protection against excessive epinephrine. In our series, ventricular fibrillation did occur in certain animals given adrenolytic drugs and in which caval occlusion had not been performed. In two dogs, an analysis of the blood from the left renal vein by a photofluorometric method † failed to reveal significant increase in epinephrine during hypothermia.

The fact that ventricular fibrillation occurs in human cases under hypothermia has been established through the experience of Bailey,‡ Swan,§ Ripstein,‖ and others. We have observed ventricular fibrillation once among 11 human cases subjected to hypothermia. This occurred in a 29-year-old man with severe tetralogy of Fallot, at a rectal temperature of 25 C. and prior to thoracotomy. Since the occurrence of this most serious cardiac arrhythmia constitutes a real danger in the clinical application of hypothermia, at least in a range below 28 C., it is important that efforts continue to determine all the factors involved in its cause and prevention. Our studies, like those of others, have suggested certain clues which should be pursued further.

SUMMARY

Hypothermia induced by surface cooling was studied in 30 dogs. Various patterns of respiratory control were employed, and the effects on the acid-base balance were noted. A metabolic acidosis developed during hypothermia which was not reversed by warming. A fall in blood pH could be prevented by control of shivering and by hyperventilation. Ventricular fibrillation occurred in seven animals, in six of these below 23 C. This serious arrhythmia did not occur in animals in which the pH was consistently elevated. No significant alterations in results of blood chemistry studies or electrolytes were observed during hypothermia. Increase in venous clotting time was observed without change in prothrombin time. The blood pressure, pulse rate, and oxygen consumption were decreased with cooling in a consistent pattern.

Drs. E. M. Papper and Duncan Holaday gave advice in the preparation of this paper.

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PROLONGED EXPERIMENTAL OCCLUSION OF THORACIC AORTA DURING HYPOTHERMIA

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ELECTIVE occlusion of major vessels proximal to vital structures in normothermic animals and humans has been limited in time because of tissue necrosis following prolonged ischemia. The known effect of general hypothermia in reducing tissue metabolism suggested the possibility of utilizing this technique as a means for prolonging regional ischemia without tissue or organ damage. The desirability of an essentially bloodless field for certain surgical procedures is obvious and has interested many clinical investigators in the past.

Raffuci and Wangensteen,[12] in 1950, found that the maximal safe period of occlusion of the hepatic artery and portal vein in normal dogs was 20 minutes. Lengthening the occlusion time produced hepatic necrosis. Burch and his colleagues,[5] in 1953, successfully resected a temporarily bloodless left lobe of the liver in two patients while occluding the aorta above the celiac axis for 10-minute intervals. Both of these reports were during normothermia. Increasing the available time would naturally be advantageous.

Occlusion of the thoracic aorta for periods of more than 30 minutes frequently results in hind-quarter paralysis. Blalock and Park [4] reported operations on 43 dogs in which the thoracic aorta was occluded for anastomosis of the left subclavian artery into the side of the distal aorta segment. The period that the aorta was occluded during the performance of the anastomosis varied from 40 to 65 minutes. One half of these dogs developed hind-quarter paralysis of varying degree during the first 24 hours after the operation. Gross and Hufnagel [10] published similar results; they noted and emphasized great variation in the tolerance of the dog to aortic occlusion. One animal was paralyzed after only 10 minutes of occlusion, whereas on occasion there was no paralysis after 50 minutes of occlusion. Beattie and others [2] observed a 40% incidence of hind-quarter paralysis in dogs when the aorta was occluded for 60 minutes. In a series of 15 dogs cooled to rectal temperatures of 20 to 30 C., five survived without paralysis after thoracic aorta occlusion for 90 minutes. Previously, Beattie and his co-workers [2] had reported paralysis in a human patient with coarctation of the aorta. This occurred after clamping the aorta and left subclavian artery for 38 minutes. Bing and co-workers [3] similarly observed paralysis in a coarctation of the aorta following anastomosis of the left subclavian artery to the distal thoracic aorta. One of us (HS) also had one instance of paraplegia following resection of a coarctation associated with patent ductus arteriosus. Occlusion time in this patient was 62 minutes. However, Crafoord [8] successfully clamped the aorta for a patent ductus arteriosus for 27 minutes.

The fear of hind-quarter paralysis and abdominal viscera ischemia has led to ingenious shunts, first reported by Carrel,[6] in 1910, and subsequently modified by others.* The longest period of occlusion published was 180 minutes in the patient of Shafer and Hardin.[13]

Since thoracic aorta occlusion exceeding 30 minutes in the normothermic animal is associated with a progressive incidence of

Presented at the meeting of the North American Chapter of the International Society of Angiology, San Francisco, June 19, 1954.

From the Halsted Experimental Laboratory and the Department of Surgery of the University of Colorado School of Medicine, supported in part by United States Public Health Service Grant H-1559.

* References 7, 9, and 11.

paraplegia, we have studied the effect of hypothermia on the safety of prolonged aortic clamping in 16 dogs.

PROCEDURE

Healthy mongrel dogs were deeply anesthetized with pentobarbital sodium. An endotracheal tube was inserted, and the dog was hyperventilated with pure oxygen to produce respiratory alkalosis. The animal was then immersed in ice-water until a rectal temperature of 29 C. was obtained. The dog was then removed, and after 10 to 15 minutes his rectal temperature dropped another 3 to 6 degrees. The lowest temperature was therefore between 23 to 26 C. Under aseptic technique, the left chest was entered through the fourth or fifth intercostal space. The descending thoracic aorta was isolated either in the high or in the midportion and occluded with a noncrushing clamp for either 90 or 180 minutes. The clamp was then released, and the chest was closed in layers with water-sealed drainage. The animal was then placed in a 45 C. warm-water bath until a rectal temperature of 30 C. and spontaneous respirations were obtained. Six hundred thousand units of penicillin were given postoperatively.

RESULTS

In a control series conducted by us, we found a 50% incidence of hind-quarter paralysis when the thoracic aorta was occluded between 20 and 30 minutes in 36 normothermic dogs.

Sixteen dogs were subjected to occlusion of the thoracic aorta while their rectal temperatures were in the range of 23 to 26 C. A noncrushing clamp was placed across the upper third of the vessel in seven dogs. In five of the animals, the aorta was occluded for 90 minutes, while the arterial flow was obstructed in the remaining two for 180 minutes. In a second series, the middle third of the thoracic aorta was occluded, for 90 minutes in seven animals and for 180 minutes in two. No neurological changes were observed in any of the 16 dogs (Table).

In three of these animals, renal function was studied by observations of glomerular filtration rate (using creatinine clearance) and renal plasma flow (paraaminohippuric acid). These observations were made 24 hours before and again 24 hours after operation. No significant change was found in the postoperative studies, thus suggesting that no renal damage had occurred.

Results of Prolonged Occlusion of Thoracic Aorta During Hypothermia

Point of Occlusion	Dogs, No.	Time Occluded, Min.	Results	Comment
Upper third of thoracic aorta	5	90	Survived	No complications; neurological normal
	2	180	Survived	Neurological normal; bleeding in wound at 2 hours; bloody mucus diarrhea 24 to 48 hours
Middle third of thoracic aorta	7	90	Survived	No complications; neurological normal
	2	180	Survived	Neurological normal; bleeding in wound at 2 hours; bloody mucus diarrhea 24 to 48 hours

Oozing of blood in a previously dry wound was observed in all animals after the aorta had been occluded for more than two hours, necessitating further ligation of vessels. Bloody mucus diarrhea lasting 24 to 48 hours postoperatively was also observed. Complete recovery of normal bowel function occurred in all such animals. There were no deaths in the series.

COMMENT

In view of the findings previously reported by other investigators and our work recorded here, we believe there is a possibility that major abdominal surgery may be performed in a bloodless field by occlusion of the aorta above the celiac axis during hypothermia. In addition, vascular surgery necessitating occlusion and/or replacement of the thoracic aorta may be safely performed on a patient during hypothermia. In this manner, radical procedures might be undertaken with greater

safety; there would be need for fewer blood transfusions, and there would be a reduction in operative time. These would include operations not only on the intestinal tract, but also on the liver, such as primary or metastatic tumors which, heretofore, have not lent themselves to safe, bloodless resection.

The results obtained in this study would seem to indicate that regional ischemia produced by occlusion of the thoracic aorta during hypothermia of 23 to 26 C. body temperature is possible without serious sequelae for periods up to two hours since the probable mechanism is the well-known reduction of metabolic requirements during hypothermia.

SUMMARY

In normothermic dogs, occlusion of the thoracic aorta for progressive periods is associated with a variable but increasingly important incidence of paraplegia.

Sixteen dogs were subjected to occlusion of the upper or middle thoracic aorta while their body temperatures were in the range of 23 to 26 C., for periods of either 90 or 180 minutes.

Studies of renal function, neurological evaluation, and signs of general well-being indicated no permanent tissue damage resulting from those procedures.

All 16 of the dogs survived both thoracic aorta occlusion times studied. No complications were observed in the 90-minute occlusion group. However, those occluded 180 minutes showed a controllable bleeding tendency in the wound site after two hours and a bloody mucus diarrhea persisting for 24 to 48 hours postoperatively.

It is concluded that occlusion of the thoracic aorta during hypothermia for periods up to two hours is sufficiently safe to warrant clinical trial.

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SOME PRACTICAL ASPECTS OF ANTICOAGULANT THERAPY

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ANTICOAGULANT therapy at the Royal Victoria Hospital in Montreal is directed by the personnel of the hematology service. Certain technicians are highly trained in coagulation techniques and perform the prothrombin and clotting determinations. The hematologist in charge of anticoagulant therapy not only supervises the laboratory tests but is continually aware of the clinical condition of the patient; he advises as to initiation and cessation of anticoagulant therapy, selects the anticoagulants to be used, and orders their daily dosage. This has resulted in extensive experience in the clinical and laboratory aspects in managing a wide variety of patients.

As a prerequisite to starting anticoagulant therapy, each patient is assessed clinically as regards indications and contraindications, and preliminary hematologic studies are performed as indicated. Heparin is usually administered intravenously every four hours. The three-tube modified Lee-White clotting time is performed initially, two and one-half hours after the first heparin injection and twice daily thereafter, in each instance two and one-half hours after the last previous heparin dose. Prothrombin times are performed initially and at least once daily thereafter, except on patients who are well stabilized on long-term ambulatory treatment.

The reliable estimation of these tests is essential as they are the principal criteria for the designation of anticoagulant dosage.

Quick's one-stage method has been used in our laboratory, with commercial dried rabbit brain thromboplastin. It is a simple, satisfactory method for clinical purposes, provided its technique is carefully controlled.

As yet, we have not found it desirable to adopt the method of Owren [1] and of Frommeyer,[2] as modified by Ware.[3] Accurate performance of the prothrombin time and an awareness of technical pitfalls such as the variability of different batches of thromboplastin, the alteration of thromboplastin on standing for several hours at room temperature, the apparent increase of prothrombic activity of a given sample of plasma on standing more than a few hours, the rapid deterioration of factor V when plasma stands, the necessity of using an optimal amount of calcium in the test, the effect of the presence of circulating anticoagulants and of fibrinogenopenia, and the necessity of using an accurate prothrombin dilution curve as a standard would all seem of greater importance than the precise test used. Initially it is also important to recognize that the prothrombin time changes only slightly in the range of 50 to 100% of normal prothrombic activity and that the optimal dosage for a patient with 50% initial prothrombic activity differs from that of a patient with initial activity of 100%. Consequently, it is helpful to perform both the whole and dilute plasma prothrombin times when prothrombic activity is above 50%. The method of expressing the results of the prothrombin test vary. In some hospitals, the results are given as prothrombin time, and anticoagulant therapy is aimed at prolonging the time to two, two and one-half, or three times that of the normal control. This is probably a useful "rule of thumb," but we believe that it is not entirely safe. Formerly we converted "prothrombin time" to "prothrombic activity" by reference to a standard curve obtained by diluting pooled normal plasma with saline (Fig. 1).

From the Hematology Service of the Department of Medicine, the Royal Victoria Hospital.

Presented at the meeting of the North American Chapter of The International Society of Angiology, San Francisco, June 19, 1954.

PROTHROMBIN DILUTION CURVES OF FRESH POOLED NORMAL PLASMA.

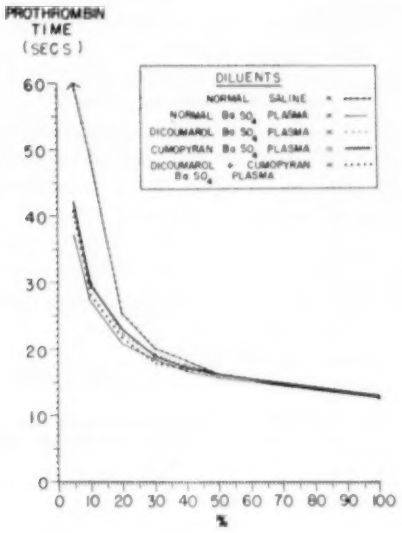


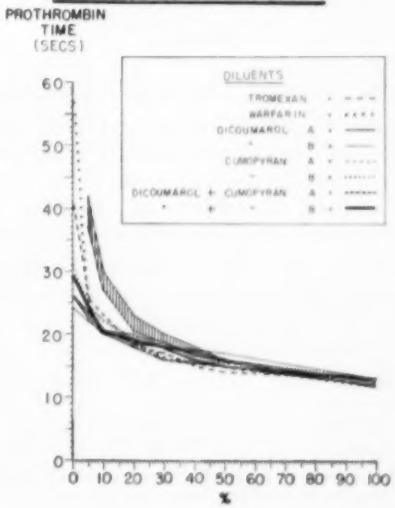
Figure 1.

The validity of using saline as a diluent for construction of such a curve has been questioned by various workers, and alternative diluents recommended are plasma adsorbed with barium sulfate, aluminum hydroxide or calcium triphosphate, and bishydroxycoumarin (Dicumarol) or biscoumacetate (Tromexan) plasma. These comparative results are seen in Figures 1 and 2, and it is apparent that the differences are fairly marked in the higher dilutions. These differences become increasingly more marked in the therapeutic range of 10 to 30% prothrombic activity. Thus a given prothrombin time, which may be within the so-called safe therapeutic range using saline as a diluent, is actually well within the danger zone if prothrombic activity is interpolated from curves using normal or anticoagulant plasma, adsorbed with $BaSO_4$, as a diluent. Many experiments were performed comparing the dilution curves of pooled normal barium sulfate-adsorbed plasma and pooled barium sulfate-adsorbed plasma from patients on anticoagulant therapy. As in Figure 1, at 40% or greater dilution the prothrombin times of adsorbed normal plasma were uniformly slightly shorter than the prothrombin times of adsorbed anticoagulant plasma. On the other hand, when unadsorbed anticoagulant plasma was used as a diluent the prothrombin times in the high dilutions were always shorter than the prothrombin times of adsorbed normal plasma. From these studies it would seem apparent that saline and unadsorbed anticoagulant plasma should not be used as diluents for standard reference curves and that there is so little difference between the curves obtained with adsorbed normal and adsorbed anticoagulant plasma that either may be used for reference standards.

From Figure 3 it may be seen that when $BaSO_4$-adsorbed plasma is stored frozen and used as a diluent for fresh normal pooled plasma, the prothrombin times above 20% dilution become progressively prolonged with increasing length of storage. Hence, it is inaccurate to use $BaSO_4$ plasma as a diluent if it has been kept in the frozen state for longer than two days. On the other

Figure 2.

EFFECT: DILUTION OF NORMAL PLASMA BY PLASMA FROM PATIENTS ON ANTICOAGULANT THERAPY



hand, the test plasma may be stored in the deep freeze for 48 hours or longer without significantly affecting the prothrombin time (Fig. 4) so long as relatively fresh $BaSO_4$ plasma is used as a diluent; at room temperature or 4 C., however, the prothrombin times are rapidly altered after several hours (Fig. 5).

The data from 275 patients treated during a 12-month period is grouped for purposes of review as shown in Table 1.

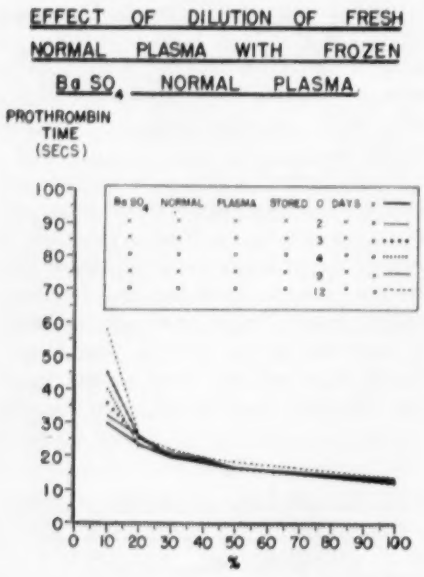


Figure 3.

We have tabulated (Table 2) the patients in whom bleeding occurred during anticoagulant therapy and compared the pro-

TABLE 1.—*Anticoagulant Therapy**

	No. Cases	Vitamin K_1	Bleeding
Coronary thrombosis	97	7	4
Thrombophlebitis	66	3	2
Arterial occlusion	27	3	2
Pulmonary embolism	16	2	0
Cerebral thrombosis	7	0	1
Retinal thrombosis	3	0	0
Obst. and gynec.	40	0	8
Prophylactic	19	3	1
Total	275	18	18

* April 1, 1953–March 31, 1954.

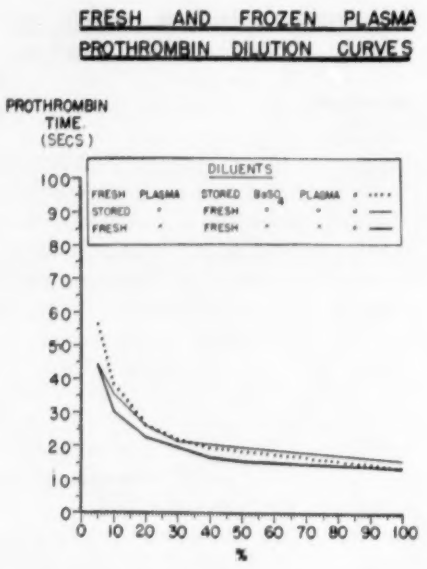
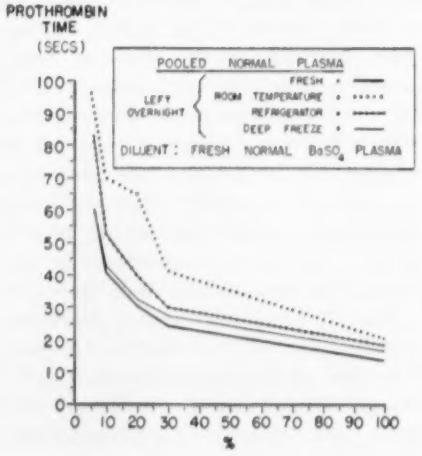


Figure 4.

thrombic activity in each case, using saline and $BaSO_4$ plasma dilution curves. With the saline curve, bleeding occurred when the prothrombic activity was in the therapeutic range of 10 to 30% or higher in each case, but with the same prothrombin time, and

Figure 5.



utilizing the $BaSO_4$ plasma curve, five of the patients had less than 10% prothrombic activity. As noted by others,* the most impressive finding is that bleeding occurred most frequently when prothrombic activity was well above the so-called danger zone. Nevertheless, it is significant that when the adsorbed plasma dilution curve is used as a standard of reference, the dosage required to maintain the so-called therapeutic range is different from that required when the saline dilution curve is used.

The indications and contraindications for anticoagulant therapy have been repeatedly reviewed [8] and will not be generally discussed in this paper. The physician is now offered a fairly wide selection of anticoagulants, each of which has its own merits. Our own experience is greatest in the use of bishydroxycoumarin, and we feel that it is still one of the best in all respects. Its chief shortcoming is the lag of 36 to 48 hours before there is significant effect on the prothrombin time. To overcome this and following the lead of others,† we have used bishydroxycoumarin in combination with heparin and/or biscoumacetate or, at times, phenindione (phenylindandione) where rapid anticoagulation is necessary. This is illustrated in Figure 6: a patient with myocardial infarction received both biscoumacetate and bishydroxycoumarin for the first 48 hours to produce a rapid decrease of prothrombic activity and was then maintained on bishydroxycoumarin alone. In patient M. M. (Fig 7) with postpartum phlebitis, heparin was used intermittently, 50 mg. every four hours until biscoumacetate had resulted in a drop in prothrombic activity. After 48 hours, it was possible to carry on with bishydroxycoumarin alone.

TABLE 2.—*Hemorrhagic Complications of Anticoagulant Therapy*

	Case No.	Site or Condition	Severity	Prothrombin Time,* Seconds	% Prothrombic Activity	
					Saline	$BaSO_4$ Plasma
Coronary thrombosis	44	Menorrhagia	+	22	26	12
	57	Epistaxis	+	29	16.5	7
	58	Hemoptysis	++	25	13	5.5
	78	Epistaxis	+	26	19	8.5
Thrombophlebitis	7	Hematemesis, hematuria	+++	21	28	13.5
	31	Rectal, vaginal	+++	16	45	23
Arterial occlusion	13	Epistaxis	+	21	28	13.5
	22	Upper G. I.	+++	20	30	15
Cerebral thrombosis	6	Rectal	+	27	18	8
Prophylactic	8	Perineal wound	+++	27	18	8
Obst. and gynec.†	18	Vaginal P. O.	++	19 †	50	68
	24	Vaginal P. P.	+	26	33	24
	28	Vaginal P. O.	+++	34	19	13
	34	Vaginal P. P.	?	25	35	27
	39	Vaginal P. O.	?	23	40	40

* Normal, 12 seconds.
† Normal for obstetric and gynecologic group, 15 seconds.

Biscoumacetate and phenylindanedione may be used alone and have been considered safer than bishydroxycoumarin because of their more rapid excretion. Probably because of this feature we have found it more difficult to maintain a smooth level of prothrombic activity with the former substances. This is illustrated in patient G. N. (Fig. 8). It is granted that this patient had various complicating features that made control more difficult. Cyclocumarol ‡ has been used by us in 30 patients; therapeutic prothrombin time

* References 4 and 7.

† References 5 and 6.

‡ Since submission of this article for publication an additional 120 patients have been treated with cyclocumarol with equally satisfactory results. This series will form the basis of a separate report.

levels were usually obtained within 48 hours; ease of maintenance compared favorably with bishydroxycoumarin. Warfarin sodium given intravenously, especially, is proving useful postoperatively and in patients who cannot tolerate oral medication.

This same patient (Fig. 8) demonstrates that a prolonged depression of prothrombic activity may follow average doses of anticoagulant drugs. This proved to be a terminal illness, and diabetes, hepatomegaly, and anemia were complications. We have been aware that the amount of anticoagulant required was influenced by the patient's clinical state, especially in patients with myocardial infarction. An attempt has been made to analyze some of these apparent factors (Table 3*A*). Patients selected were those who had initial hypoprothrombinemia and those who required less or more than average amounts of bishydroxycoumarin, using about 50 mg. of bishydroxycoumarin daily as the average maintenance dose. Patients who required oxygen therapy, those who were in circula-

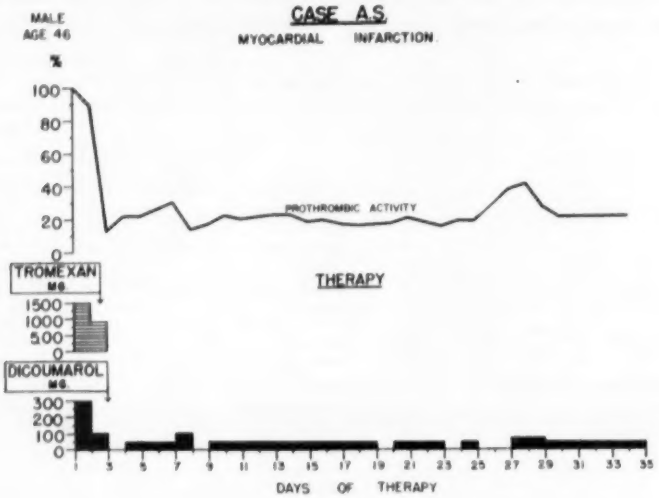


Figure 6.

TABLE 3.—*Factors Influencing Response to Anticoagulants*

	Hypoprothrombinemia Before Anticoagulant	Dose Less Than Average	Dose Greater Than Average
A. Coronary Thrombosis			
Oxygen therapy	4	9	0
Congestive failure	3	6	1
Shock	1	0	0
Hepatomegaly	0	3	0
Liver damage	1	0	1
Diabetes	0	3	2
Infection	0	3	1
Miscellaneous	2	6	1
No apparent reason	0	5	6
B. Thrombophlebitis			
Pulmonary infarction	1	3	1
Infection	3	2	0
Diabetes	0	2	1
Liver damage and hepatomegaly	3	0	0
Pancreatitis	3	3	0
Carcinomatosis	2	3	0
Gastric resection	3	3	1
Miscellaneous	6	4	10

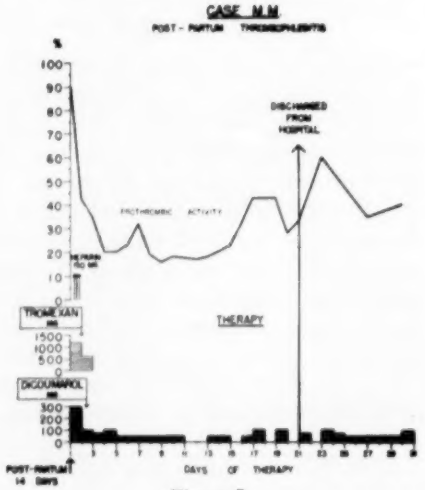


Figure 7.

tory collapse, and those with congestive failure were more often hypoprothrombinemic and bishydroxycoumarin-sensitive. Liver enlargement, diabetes, and infection also seem of some importance. These data are probably not susceptible to statistical analysis but appear to bear out a "clinical impression"—admitting the dangers of clinical impressions. It is our impression that a patient with a fresh myocardial infarct, who is in congestive failure and sufficiently sick to warrant placing him in an oxygen tent, will require relatively small doses of anticoagulant, although hyperprothrombinemia has been reported in myocardial infarction.

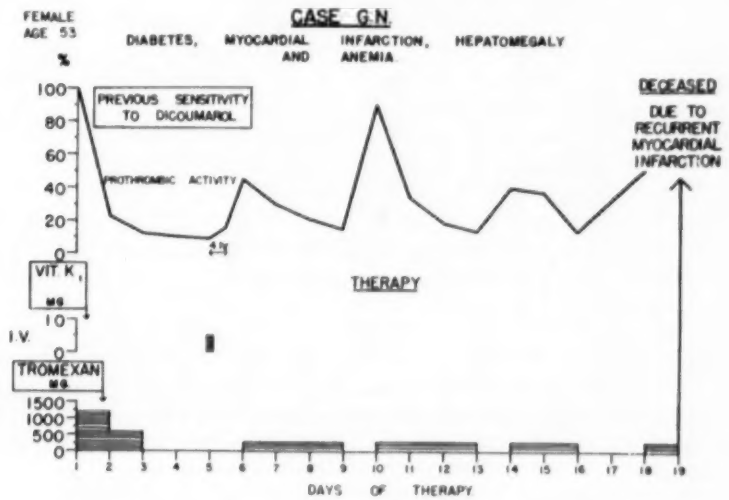


Figure 8.

The factors influencing dosage in the group of thrombophlebitis cases were also analyzed (Table 3*B*). No one factor appears outstanding, but the presence of liver damage, pancreatitis, or recent gastric resection appear to have some effect.

The danger of hemorrhage in anticoagulant therapy has always acted as an inhibitor to treating patients with anticoagulant drugs. We have had our share of bleeding complications, both minor and major (Table 2)—15 cases in 275 treated, or 5.4%.

Vitamin K_1 is capable of reversing depressed prothrombic activity very rapidly, except in the presence of severe parenchymal damage of the liver. We have used intravenous vitamin K_1 in 18 instances, either because of unduly prolonged prothrombin time and/or because of bleeding. In 14 of these, prothrombin time was determined at 4 hours and 24 hours (Fig 9). Doses of 5 to 50 mg. of K_1 were given intravenously. The amounts given shortened the prothrombin time to normal. Doses of the order of 1.0 to 2.5 mg. seem to shorten the prothrombin time to the therapeutic range. The prothrombin time is significantly altered four hours after administration of K_1 intravenously, and increased resistance to bishydroxycoumarin and related compounds may persist for several days after administration of vitamin K_1, thus causing difficulty in anticoagulant control.

CONCLUSIONS

An effectual working scheme for anticoagulant management of thromboembolism is outlined, which depends on unified laboratory and clinical control of therapy.

Some practical laboratory aspects of prothrombin time determinations are discussed. When the Quick method or its modifications are used for prothrombin time determina-

tions, freshly adsorbed prothrombin and factor VII free plasma should be used as a diluent for standard reference curves of prothrombic activity in preference to saline.

As a result of study of the complications of anticoagulant therapy of 275 cases over a 12-month period, there was an impression that patients with myocardial infarction who require oxygen, or who are in circulatory collapse or congestive failure, and patients with thrombophlebitis complicated by liver damage, uncontrolled diabetes, infection, or pancreatitis often exhibit initial hypoprothrombinemia and are sensitive to the bishydroxycoumarin group of anticoagulants.

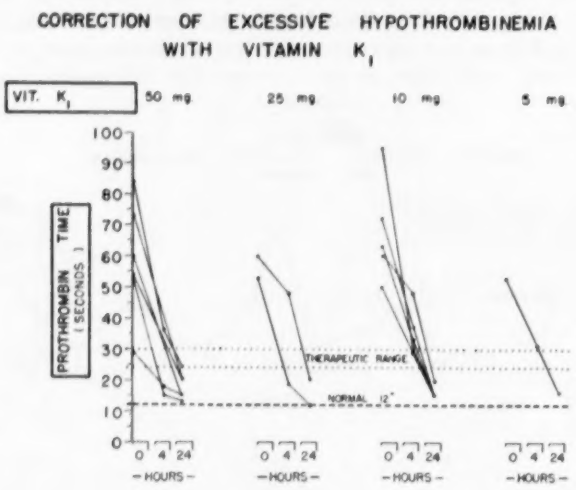


Figure 9.

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REPLACEMENT OF ARTERIAL SEGMENTS, UTILIZING FLEXIBLE ORLON PROSTHESES

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BEGINNING in 1944 and in the ensuing years we have been active in the investigation of the problems of arterial homografts. Early in this work we felt the need for some method for preserving such grafts for use at a time considerably after their removal. Initially, we advocated the use of rapidly frozen grafts and showed that such grafts could be kept for prolonged periods of time at temperatures of —70 C.* Later the rapid freezing process was supplemented by drying in the frozen state,[3] and after this we devised the method for the sterilization of such grafts with the use of ethylene oxide, both as a liquid and as a gas.[4] The culmination of this process has therefore been the use of freeze-dried grafts which can be kept indefinitely in sealed vacuum tubes after being taken without aseptic precautions.

For the past two years all the homografts which we have used in patients have been processed in this manner. Later we extended this process to heterografts and have conducted considerable investigation in this field. From the inception of this work with homografts, however, it has been our desire to eliminate the use of grafts as such and to substitute material of completely nonbiologic origin. We have used plastics from the beginning of this investigation because they appeared to be most suitable in terms of general tissue reactivity and surface properties. When such plastic materials first became available they were always rigid in form. As progress has been made they have been available in more and more flexible varieties. We have been impressed that the surface properties of the materials employed have a distinct effect upon the relationship to thrombosis.

Among the properties which have appeared to be important have been tissue tolerance, the wetability of the surface, the surface charge, the wearability of the material, and, finally, the smoothness of the surface. When using rigid types of protheses it was necessary to use a new method of fixation of the prosthesis within the blood vessel. The method which has been most satisfactory in our hands we have termed "multiple point fixation." However, rigid tubes have certain disadvantages which are inherent. The fit of such tubes must be quite exact, their length cannot be altered readily, and in the case of tapering vessels it is frequently difficult to have a sufficient number of tubes available to meet the varying demands. Rigidity makes the tubes much less suitable for crossing of major flexion creases, or in other sites in which mobility is a major factor.

Voorhees, Jaretzki, and Blakemore[5] experimented with Vinyon-N, which is a flexible type of cloth. We have followed this with a study of a number of plastic materials in an attempt to evaluate the usefulness of this type of prothesis and in an attempt to find materials which avoided some of the disadvantages of Vinyon. During the past two years we have therefore investigated varying weaves of different plastic materials in an effort to accomplish this. Among the materials which have been investigated have been a polymer of acrylnitrile (Orlon), varying forms of nylon, Orlon coated with silicone, Dacron, and glass fiber. In an effort to establish what materials might be the most suitable, we first selected them on the basis of their physical properties. Of

From Georgetown University Medical Center.

Presented at the meeting of the North American Chapter of The International Society of Angiology, June 19, 1954, San Francisco.

* References 1 and 2.

the group tested, Orlon and some forms of Dacron appeared to have the most desirable surface properties. It seemed of considerable importance to us from the outset that the type of fiber employed would be significant. We elected to select multifilament types of fiber in which there was very little irregularity of the individual strands, and in which individual strands were quite long without a break. This would give a smooth surface. Monofilament types of fibers have not been available in a sufficiently fine weave to be highly applicable; however, such monofilament fibers are available in the form of seamless tubes, whereas multifilament fibers are much less readily available in this form. For such a tube to be widely useful it is quite apparent that the leakage of blood through the interstices of the tube must be minimal. Blakemore and Voorhees have attempted to avoid this by allowing blood to come in contact with the material prior to its implantation, laying down fibrin in the interstices of the fibers. If one does not do this, the leakage from Vinyon in high-pressure areas is considerable and may be difficult to control except by allowing sufficient time for the blood to clot. In order to do this it is of course necessary to interrupt the blood flow or clotting will not occur readily. We have felt that this is undesirable and have also believed that preclotting per se is not ideal. Therefore, we have attempted to select weaves in all of these materials in which the interstices between the fibers are sufficiently small that bleeding does not occur. In the case of materials which have marked hemorepellency these interstices can be considerably larger than the actual size of a blood cell without leakage, because of the repelling property of the surface of the material. It is desirable to have the individual fiber size small; that is, the number of multistrand fibers per inch is large, in order to have the interstices of sufficiently small size.

With these preliminary considerations in mind the particular cloth to be tested was selected. The cloth was then made into a tube in one of several ways. Ordinarily the tube of the given diameter was then made by sewing cloth into a simple tubular form, using material of the same nature as the cloth. The thread used for the suturing of the tube was ordinarily approximately 00000 gauge in diameter. The ends of the tube are slightly flared and then turned back as a cuff as shown in Figure 1. This slight flaring of the ends makes it much simpler to turn back the cuff without impinging upon the lumen of the tube at the site which was elected for the anastomosis. Flaring can be a problem with fabrics unless this double cuff is used. In the initial experiments the tubes were all sewn by hand and a double suture line was used in forming the tube. It was soon apparent, however, that if one used a sewing machine with a very small needle

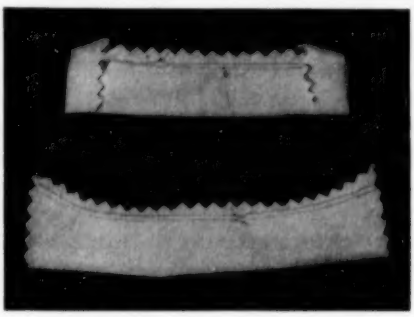


Fig. 1.—Orlon tubes with standard flared ends before and after cuff is turned back.

one could evert the longitudinal seam and trim off the excess from the seam, securing results which were identical. When this is done, a double seam should be made for additional protection and the ends of the suture should be tied rather than depending upon the simple locking stitch of the sewing machine for adequate fixation of this main longitudinal suture in the tube. The elasticity of the tube depends in some measure upon the way in which the material is woven and the direction, in relation to the weave, in which the tube is cut. Tubes made for insertion into the abdominal and thoracic aorta of dogs vary in diameter from 5 mm. to 1.2 cm. The tubes are made 4 cm. in length in the majority of cases, but in the thoracic aorta segments up to 10 cm. in

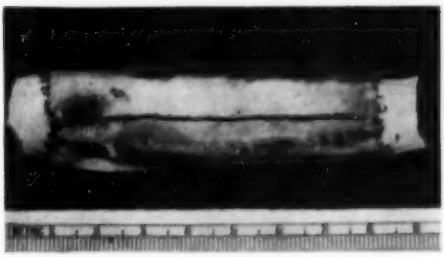


Fig. 2.—Orlon prosthesis 48 hours after implantation. Note the very thin fibrinous lining of the tube.

length were used. The weave which has been selected as being most useful generally has been 75 by 100 type 81 Orlon. This material has been tested most widely. Dacron of slightly finer weave has also been tested and has shown properties which are quite similar. The results with glass fiber are not yet complete.

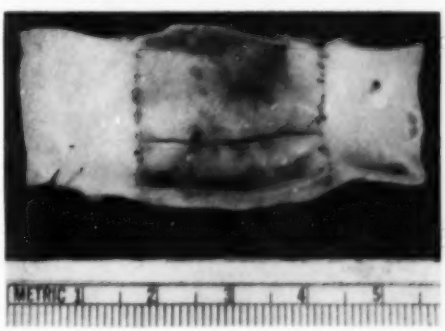
When tested in the abdominal aorta of dogs, tubes of this type from 5 to 7 mm. in diameter have given 90% patency over periods up to one year. There has been no instance of disruption of the graft nor of the aneurysm at the suture line. It is to be expected, however, that the latter complication may occur if a leak in the suture line occurs, due to tearing out of the suture; such an aneurysm is always a possibility in any vascular suture.

The primary complication which has occurred with cloth tubes has always been thrombotic in nature and has occurred in approximately 10%. We believe that vessels of this size in the abdominal aorta offer a good test of general function for such grafts, and these have shown certain fundamental problems associated with the type of cloth which is used. All cloth grafts tend to be somewhat less resilient and elastic than the normal vessel. If there is a discrepancy in size between the graft and the prothesis and it is necessary to wrinkle the prothesis in order to make the two fit, there is a tendency for fibrin to be laid down in these wrinkles until they are eliminated. At this point the process then goes on in a manner comparable to that which occurs throughout the rest of the graft. However, if the wrinkling has been great, as it has been in some of our test anastomoses, the likelihood of thrombosis is greatly increased. A similar situation also obtains in the case of a homograft when there is a disparity in size between it and the host vessel. It should be pointed out that with some forms of the fabric, particularly with the heavier types, the difficulties of suturing are somewhat greater than those of homografts.

When Orlon or nylon is used, the ends of the fabric may be sealed by heat, so that it is not essential to turn back a cuff. Seamless tubes can be made from Orlon and nylon by heat sealing, but it has been our general experience that unless this is done with considerable exactitude there is a change in the fiber produced by the heat in the adjacent areas and that when stress is applied to the seamless tube it will not resist the same degree of tension as previously. We, therefore, have elected not to rely upon heat sealing as a primary method of producing seamless tubes.

These grafts have been followed histologically throughout their course, and the changes which occur may be briefly reviewed as follows. These changes are typified by the use of the Orlon graft, in which the tissue activity is small and in which at the time of operation there is essentially no bleeding through the interstices of the tube. Immediately following implantation, during the

Fig. 3.—Orlon prosthesis 54 days after implantation, showing the thin translucent endothelial-like lining and some areas in which blood pigment has not yet been completely absorbed.



first 48 hours, there is laid down upon the inner surface of the cloth a very thin layer of homogenous material, which is fibrin-like in character. The amount of such fibrin deposited on the surface of the tube will vary with the type of material employed. With Orlon it is in extremely small amount and exists in an extremely thin layer. This does not appear to be thrombogenic. If the graft is removed at this time, one can see only a slightly pink transparent layer over the surface of the implant. Within the next two

Fig. 4.—Orlon prosthesis 104 days after implantation. Note endothelial-like inner layer.

days the layer becomes slightly thicker and redder, apparently owing to enmeshment of red cells. With the Vinyon type of cloth it has been our experience that the layer which is laid down is distinctly thicker and becomes red with enmeshment of red cells very early and to a distinctly greater degree. In approximately two weeks one begins to see islands of what appear to be endothelial-like cells scattered throughout the entire length of the graft. They do not appear to grow in from the ends but are irregularly grouped and tend to coalesce gradually. The various stages of this process are shown in Figures 2 and 3. As this process continues the pink color is lost from the surface of the graft and it becomes whitish and translucent; it is sufficiently thin that one can grossly see the individual fibers of the prosthesis through the overlying endothelial-like layer.

Microscopically the surface of the graft is first covered with a fibrinoid material; later this shows enmeshment of red cells, and gradually islands of flattened endothelial-like cells appear on the surface; this process then continues, with coalescence of these areas to form a layer within the Orlon and a fibrous layer outside it. The endothelial-like layer is associated with several layers of flattened cells immediately beneath it. Some fibers appear to grow through the spaces in Orlon, although these are quite fine and tenuous in character. With some types of material the inner layer appears to be separated into two component parts, similar to those which are seen in the normal intimal layer of an artery. The fibrous tissue layer which surrounds the outside of the tube is also composed of relatively small number of layers of fibroplastic cells (Figure 4).

COMMENT

Tubes of this type have been used experimentally during the last two years in the abdominal and thoracic aortas of dogs. In the course of these experiments silicone was used to coat the graft in an attempt to render it more water-repellent. However, it was found after a trial with this material that some difficulty with thrombosis was encountered because the graft was not adequately washed. Later experiments showed that silicone apparently added little to the over-all result, and introduced a new element of possible variation. With the proper type of Orlon material we feel that we have found that uniform patency can be obtained in vessels down to the size of the abdominal aorta of the dog. Experiments are now under way to test it in smaller vessels.

Orlon is sterilized by autoclaving. This sterilization by heat does not adversely affect

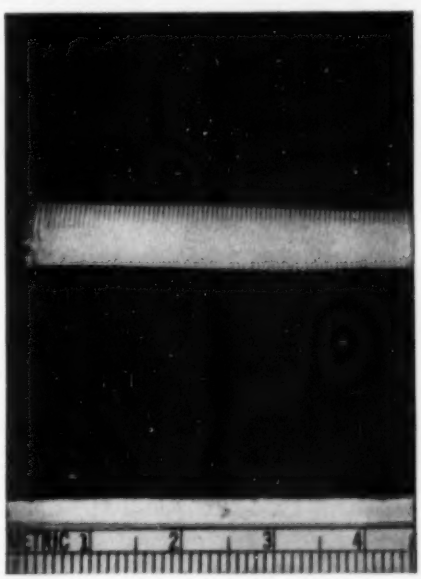
Fig. 5.—An occluded segment of the external iliac artery has been resected and replaced with an Orlon tube.

the Orlon and tends to shrink the fibers slightly, making it less permeable to blood. When the material is sterilized by soaking, the interstices are slightly larger than optimum and considerable leakage may occur when blood flows through the tube. After periods up to two years no fragmentation of the material has been observed and it is completely encapsulated within the surrounding tissue. Once the process of "reendothelialization" has occurred, we have never observed thrombosis. As more experience has been gained in the use of such tubes the incidence of thrombosis has been greatly reduced, until it is now comparable to that which is obtained with homografts.

Encouraged by this success with the experimental work, we have now implanted 15 protheses of this type to replace the abdominal aortic bifurcation in cases of aneurysm and chronic occlusion. We have also used it in the common iliac arteries and in the femoral arteries. The first graft was placed approximately 16 months ago in a patient, and it has remained patent. We have had no incidence of thrombosis in either the large or the small grafts and no complications of hemorrhage or aneurysm formation. Figure 5 shows the external iliac artery replaced with an Orlon prothesis. In the majority of the patients in which Orlon has been employed the entire abdominal aorta from just below the renal arteries down to and including both branches of the common iliacs has been utilized. The grafts for human use are available in several sizes and may be made directly at the time of operation, if the proper size is not available.

Currently, we are attempting to find materials which are more easily handled and which have a more normal type of elasticity both in length and transverse stretch. This is best found in seamless materials which have a diagonal type of weave, and such materials are being utilized experimentally, with considerable promise (Figure 6). We feel that the advantages of ready availability and the lack of degenerative changes in the lining of the vessel wall during the time period observed in protheses of this type will

Fig. 6.—Seamless tube of Orlon, shown before a cuff has been turned.



offer a considerable advantage for widespread application of arterial reconstruction for trauma, aneurysm, and arterial occlusion and in the resection of major vessels in block dissections for tumor.

SUMMARY

The experimental background for the development of readily available tubes of Orlon has been described. The process of the deposition of fibrin and the formation of an intima-like layer of tissue on the inside of the fabric and an adventitia-like layer on the outside has been illustrated. The use of such Orlon protheses for the replacement of the aortic bifurcation, the iliac arteries, and the femoral arteries in man over a period of 16 months' observation, with no failures, has been mentioned. Finally, a description of an improvement in the type of weave which will simplify the procedure of anastomosis has been given.

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VAGUS NERVE AND PULMONARY EMBOLISM

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THE ROLE which the vagus nerve plays in the production of reflex pulmonary vasoconstriction associated with pulmonary embolization has been studied by numerous investigators. De Takats and his colleagues [1] found that atropine relieved the dyspnea produced by precapillary emboli in rabbits. They also lowered the fatality rate from massive pulmonary emboli in dogs by vagectomy and atropine. However, inferences drawn from mortality rates or symptom relief may be misleading. Studies on the hemodynamics of pulmonary embolism have demonstrated no marked changes with vagectomy.* These studies have all been undertaken with anesthetized animals or heart-lung preparations. Since it is well known that anesthesia affects the pulmonary circulation,[6] it was felt that the problem should be approached on intact animals without anesthesia.

In a previous study, graphite particles were injected into rabbits and their distribution studied in lung sections in order to determine the effect of anesthesia on vasoconstriction. It was felt that this method would be suitable for studying the relationship of the vagus nerve to the pulmonary circulation after embolization.

METHOD

Rabbits averaging 4 to 10 lb. (1.8 to 4.5 kg.) were used as the experimental animal. A 0.48% solution of 5μ sized graphite particles (Dixon's Airspun Micronized Graphite, Type 200-09) was used for embolization in a dose of 1 cc. per pound of body weight. Polyoxyethylene monolaurate (Tween 20) was used as a mixing agent for this solution.

Twelve control animals were embolized with the graphite particles. Eleven animals were subjected to cervical vagectomy under pentobarbital (Nembutal) anesthesia, and four or more hours later, when they were no longer anesthetized, they were embolized with the graphite particles. Ten animals were injected intravenously with 2.17 mg. of atropine, and 15 minutes later were injected with the graphite solution. Fifteen minutes after the graphite

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Micronized graphite was supplied by the Joseph Dixon Crucible Company, through the courtesy of Mr. E. S. Glauch, Manager.

* References 2 through 5.

Summary of Experimental Data

Control		Vagectomy		Atropine	
Animal	Arterioles per Low-Power Field	Animal	Arterioles per Low-Power Field	Animal	Arterioles per Low-Power Field
R14	22.2	R68	14.7	R52	3.9
R34	30.4	R69	16.5	R53	9.0
R36	30.9	R70	18.3	R54	2.4
R39	22.1	R71	11.0	R55	6.5
R41	22.6	R72	9.5	R57	7.6
R43	23.1	R75	11.6	R85	1.4
R46	42.3	R88	7.4	R86	0.4
R50	17.3	R89	19.2	R87	5.4
R58	10.6	R92	16.5	R90	5.1
R66	16.6	R93	12.6	R91	4.9
R74	14.1	R94	24.6		—
R77	12.1		—	Average	4.7
	—	Average	14.7		
Average	22.9				

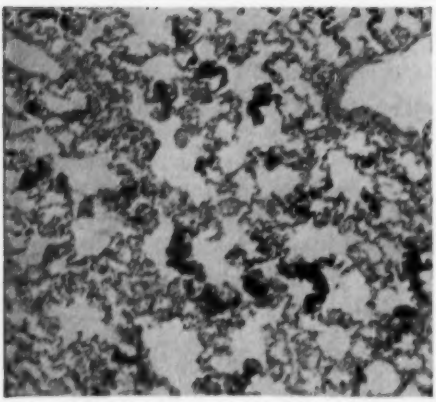


Fig. 1.—Representative microscopic lung section of vagectomized rabbits injected with precapillary graphite emboli, demonstrating clumping of graphite particles in the arterioles; × 70.2.

embolization, all animals were killed with an air embolus and lung sections taken for microscopic study.

The average number of graphite-filled blood vessels, 20 μ or larger in diameter, per low-power field was used as an index of vasoconstriction. With vasoconstriction the graphite particles collect in the arterioles, and the number of graphite-filled arterioles per low-power field is relatively high. In the absence of vasoconstriction, the graphite particles diffuse into the capillaries, and the number of graphite-filled arterioles is low. In this manner the microscopic data can be presented in tabular form.

RESULTS

The table summarizes the data obtained in this experiment. The number of arterioles per low-power field in the control animals ranged from 12.1 to 42.3, with the average 22.9. The number of arterioles per low-power field in the vagectomized animals ranged from 7.4 to 24.6, with an average of 14.7. Figure 1 is a representative microscopic section of this vagectomized group and demonstrates the clumping of the graphite particles in the arterioles. The number of arterioles per low-power field in the atropinized animals ranged from 0.4 to 9.0, with an average of 4.7. Figure 2 is a representative microscopic lung section from this group, demonstrating the diffusion of the graphite particles into the capillaries of the alveolar walls.

INTERPRETATION

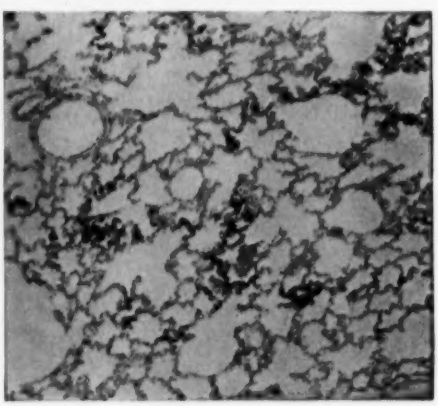
When the number of graphite-filled arterioles per lower-power field is used as an index of vasoconstriction, it would appear that vagectomy did not markedly change the response of rabbits' pulmonary arterioles to precapillary emboli. This agrees with the results based on pulmonary hemodynamics and would seem to indicate that the vagus nerve plays no role in the production of vasoconstriction associated with such emboli.

Atropine almost completely abolished the vasoconstriction associated with pulmonary emboli. It is very similar to the previously reported effect of anesthesia.[6] The reason for this result is not completely clear. Since vagectomy had no such effect, it can certainly be reasoned that the atropine response is not mediated by the vagus nerve. It must affect the blood vessels directly, and in this regard these findings compare with those of Hamet.[7] This investigator found that atropine in 2 mg. doses injected into adrenalectomized and nonadrenalectomized dogs produced a vasodilation of the vessel wall.

SUMMARY

The pulmonary vascular response to precapillary emboli (graphite particles 5 μ in diameter) was studied in control, vagectom-

Fig. 2.—Representative microscopic lung section of atropinized rabbits injected with precapillary emboli, demonstrating a relative absence of vasoconstriction, permitting the particles to diffuse through the capillaries; × 70.2.



ized, and atropinized rabbits. Vagectomy does not alter markedly the vascular response to such emboli. Atropine, however, abolishes the vasoconstriction associated with the precapillary embolization. It apparently does this by direct action on the blood vessel and not by way of the vagus nerve.

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SURGICAL CORRECTION OF EVENTRATION OF DIAPHRAGM IN PATIENT WITH ARTHROGRYPOSIS

Observations on Cardiac Manifestations of Traction on Diaphragm

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IT IS THE purpose of this presentation to discuss the management of an eventration of the diaphragm in a patient with arthrogryposis (amyotonia congenita). The association of nodal rhythm and apnea with traction on the diaphragm and mediastinum were of interest. Also noteworthy was the absence of a portion of the chest wall musculature.

REPORT OF A CASE

M. A., a one-year-old white girl, with arthrogryposis, was admitted on Aug. 7, 1952, to the Jewish Chronic Disease Hospital. Her parents and two older sisters are alive and well. At birth, it was noted that the infant had a fracture of the right shoulder, a cleft palate, clubbed feet, and flexion contractures of the wrists.

Physical examination revealed ptosis of the right eyelid, with normal extraocular movements. There were flexion deformities of both wrists, thumbs, and all fingers of the left hand, as well as clubbing of the feet. The blood pressure was 90/60. Examination of the heart revealed a regular sinus rhythm and displacement of the apical impulse to the left. Lung fields were clear to percussion, and auscultation and examination of the abdomen were not remarkable.

Complete blood counts were repeatedly normal. Urinalyses showed occasional traces of albumin and a few red and white blood cells per high-power field. Chemical examinations of the blood, which included the carbon dioxide-combining power, chloride, sodium, potassium, cholesterol, creatinine, calcium, phosphorus, fibrinogen, and glucose tolerance test, were all normal. Histologic examination of the muscle from the thigh and diaphragm was not remarkable.

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Chest x-ray revealed a well-defined paracardiac shadow which filled the right cardiophrenic angle and displaced the heart and mediastinum far to the left (Fig. 1). On fluoroscopy, both diaphragms were seen to descend without paradoxical motion. A pneumoperitoneum (Dr. A. Lewitan) demonstrated that the mass was intra-abdominal and probably represented upward displacement of the liver through an eventration of the diaphragm (Figs. 2 and 3).

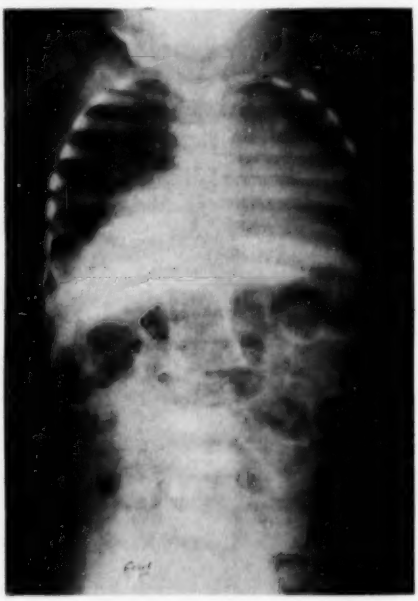

Fig. 1.—Preoperative chest x-ray shows a smooth, rounded opacity occupying the right cardiophrenic angle. It appears to be continuous with the liver shadow along its lateral aspect in the infradiaphragmatic region. The heart and mediastinal structures are displaced markedly to the left.

The preoperative electrocardiogram (Fig. 4) showed a normal axis deviation with sinus tachycardia, rate 187 per minute. A significant R wave was present in aV_L and aV_F. A tall R wave was absent in the right precordial leads (V_{3R}-V_{8R}). The QRS sequence of the precordial leads from V_1 to V_6 was normal, the tracing resembling that of the normal adult rather than of the infant.

Fig. 2.—Chest and abdominal x-ray demonstrated a pneumoperitoneum. The thinned-out medial half of the right hemidiaphragm represents the superior convex limit of the infradiaphragmatic opacity. Air is limited to the peritoneal cavity, ruling out any communication with the pleural space.

Postoperatively (Fig. 5) there was right axis deviation and a sinus tachycardia, rate 215 per minute. A deeper S_1 had appeared and R_3 had become taller. The tall R wave in aV_L became small, and the R wave in aV_F and V_1 became taller. The electrocardiogram now resembled that of the normal infant. An electrocardiogram taken three months later showed an S_1 and Q_3 with sinus tachycardia, rate 187 per minute. This resembled the one taken in the immediate postoperative period.

Because of the possibility that the mass in the right paracardial region might represent a congenital hernia or tumor of the liver, it was felt that exploration of the right chest was warranted. On Feb. 24, 1953, with the use of endotracheal ether anesthesia, an exploratory operation was done through a 12 cm. incision overlying the sixth right rib. The trapezius, rhomboids, and sacrospinalis muscles were normally developed, but the latissimus dorsi and serratus anterior were absent. A 10 cm. portion of the sixth rib was removed and the pleural cavity entered. The mass was then identified as an eventration of the anteromedial half of the right hemidiaphragm, which seemed otherwise to ascend and descend normally with respiration. The diaphragm was incised, and the dome of the liver was examined and found to be normal. A specimen from the diaphragm was then taken for biopsy and the incision closed in two layers. Four reefing sutures were so placed in the eventrated portion that when these were tied snugly, it was returned to a relatively normal position. The chest wound was then closed in layers.

From 9:35 to 10:00 a. m., during the opening of the chest wall and exposure of the right hemidiaphragm, there was sinus tachycardia, the rate varying from 200 to 250 per minute (Fig. 6*A*). With pressure on the heart and manipulation of the right leaf of the diaphragm, at 10:05 a. m., there was slowing of the ventricular rate to 150 per minute, but sinus rhythm was maintained (Fig. 6*B*). The ventricular rate returned to 214 per minute when manipulation ceased (Fig. 6*C*). With continued pressure on the heart and placement of the sutures in the right hemidiaphragm, sinus node activity was completely suppressed. A nodal rhythm, rate 125 per minute, was recorded

Fig. 3.—Left lateral recumbent view clearly outlines the lateral aspect of the liver and confirms its continuity with the more medially placed density.

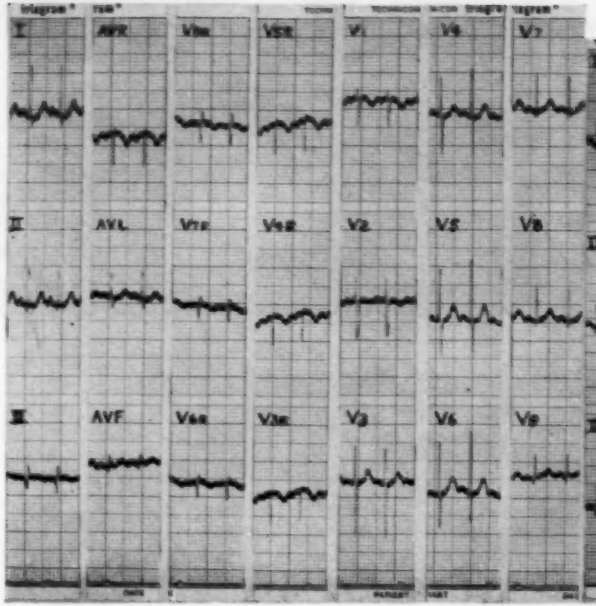

Fig. 4.—Left, preoperative electrocardiogram: sinus tachycardia, rate 187 per minute. Tall R wave in aV_L and aV_F. Absence of tall R wave in right precordial leads.

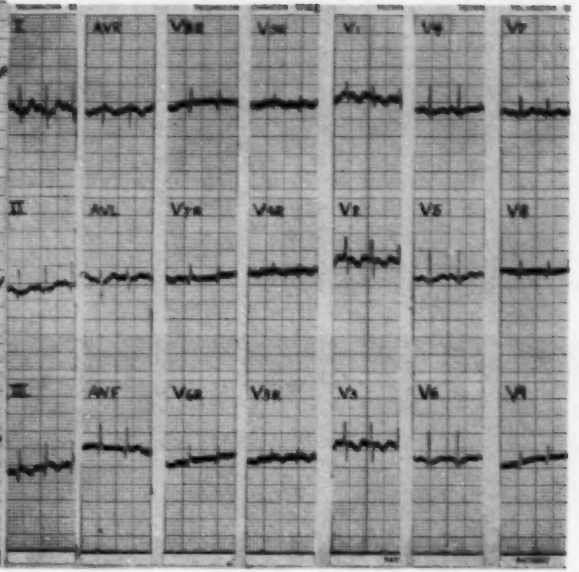

Fig. 5.—Right, postoperative electrocardiogram: S_I is deeper; smaller R waves (rS) in aV_L. Tall R waves in right precordial leads now present.

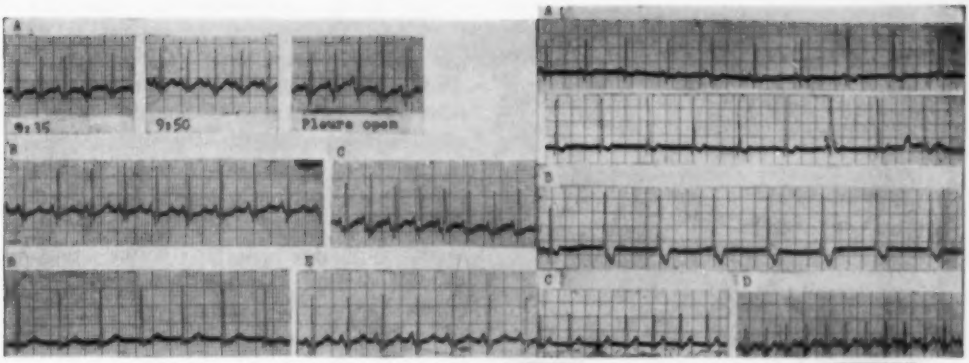

Fig. 6.—Left, sinus tachycardia: *A*, 200 to 250 per minute; *B*, 150 per minute; *C*, 214 per minute. *D*, nodal rhythm, 125 per minute. *E*, sinus tachycardia, 150 per minute.

Fig. 7.—Right, (*A*) Slowed sinus rhythm, 100 per minute, becoming (*B*) nodal rhythm, 88 per minute; deeply inverted T wave. (*C*) Nodal rhythm, 140 per minute; (*D*) sinus tachycardia, 214 per minute.

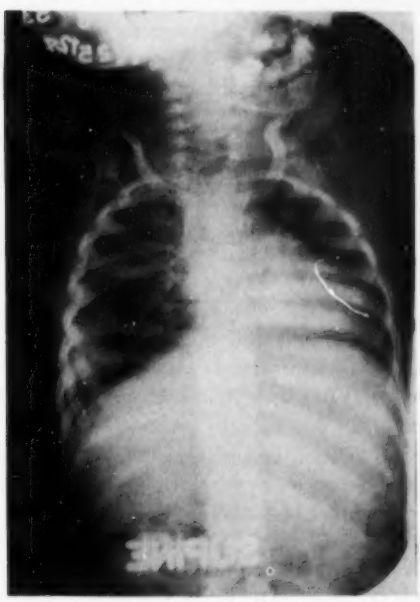

Fig. 8.—Chest x-ray one week postoperatively demonstrates correction of the eventration.

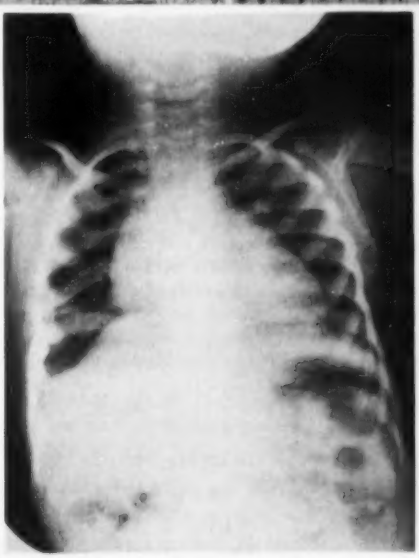

Fig. 9.—Chest x-ray six months postoperatively shows normal position of the heart.

Fig. 10.—Recent photograph of the patient demonstrates atrophy of the right shoulder girdle musculature, flexion deformity of the wrists and thumbs, clubbing of the left foot, and ptosis of the right eye.

(Fig. 6*D*). With the sutures in place, sinus rhythm returned, first at a rate of 150 per minute and then at the usual rate of 214 per minute (Fig. 6*E*).

At 10:30 a. m., when the diaphragmatic sutures were tied, and the heart was again displaced to the left, the sinus rhythm slowed to 100 per minute, and was then followed by a nodal rhythm, rate 88 per minute (Fig. 7*A*). The rate then slowed to 75 per minute. The Q wave disappeared from the QRS complex and the T wave became deeply inverted (Fig. 7*B*). At this point the operation was interrupted. It was noted that the infant was apneic. Respiration was maintained by the anesthetist until rhythmic spontaneous respiratory movements returned. A short period of nodal rhythm, rate 140 per minute (Fig. 7*C*), was followed by sinus rhythm, rate 214 per minute (Fig. 7*D*). The remainder of the procedure was uneventful, though a sinus tachycardia rate of 250 per minute was the prevailing rhythm.

The postoperative course was uneventful. An x-ray taken several days postoperatively showed the diaphragmatic reduction to be maintained (Fig. 8). A more recent x-ray (Fig. 9) demonstrates the heart to be in a normal position. Figure 10 is a recent photograph of the patient, taken six months after operation, demonstrating the ptosis of the right eyelid, marked atrophy of the right shoulder girdle musculature, flexion deformity of the wrists, and clubbing of the feet.

COMMENT

This patient with arthrogryposis had partial eventration of the right hemidiaphragm and no grossly visible serratus anterior or latissimus dorsi musculature along the line of incision. The latter abnormality is a well-recognized feature of arthrogryposis, representing either a complete atrophy with fatty replacement or a failure in development.* In our patient, biopsy of the abnormal segment of diaphragm failed to reveal any muscle abnormality. Thus, the eventration is probably unrelated to the arthrogryposis.

Eventration is a congenital aberration in the development of the diaphragmatic musculature from the septum transversum which may involve all or part of one hemidiaphragm. Usually it is unassociated with symptoms and requires no treatment. Commonly the involved portion is markedly thinned out and functions paradoxically, suggesting faulty innervation. In our case, however, there was no paradoxical motion.

The differential diagnosis of abnormal densities in the right cardiophrenic angle involves a consideration of all supradiaphragmatic and infradiaphragmatic opacities. To be considered are Morgagni hernia, mediastinal teratoma, pericardial diverticulum or cyst, tumor of the liver, or partial eventration of the diaphragm. The recommended treatment of eventration of the diaphragm is plication of the lax portion by a series of heavy reefing sutures, or incision and reconstruction of the dome in an overlapping fashion, much as in the method of Mayo for repair of ventral hernias. Operative repair, however, is rarely necessary, unless there are disabling symptoms or an exploratory operation is performed for some other reason. In our patient, operative correction resulted in satisfactory replacement of the right hemidiaphragm and liver and return of the heart and mediastinal structures to their normal position.

Displacement of the heart and mediastinal structures to the left by the abnormally elevated liver most certainly was a factor in the adult type of electrocardiogram recorded preoperatively. The absence of right axis deviation, the positivity (tall R wave) in aV_L and aV_F, and the absence of positivity (tall R wave) in the right precordial leads may be explained by the cardiac displacement to the left. Correction of displacement resulted in a tendency to right axis deviation. The usual infantile distribution of potentials was approached with positivity (tall R wave) in aV_F and in the right precordial leads.

Exploration and placement of sutures in the diaphragm necessitated pulling on the diaphragm and pushing the heart even farther to the left. Apnea and disturbances in cardiac rhythm are probably explainable by reflexes originating in the diaphragm and in the heart. It is problematical whether the afferent stimuli arise in the subpleural nerve endings of the diaphragm and mediastinum or whether displacement and rotation of the heart initiate these reflexes at the root of the great vessels which are subjected to pressure changes. Crandell and Artusio [4] reported several instances of bradycardia, hypoten-

* References 1, 2, and 3.

sion, and cardiac arrest subsequent to hilar traction which they attributed to vagal reflexes. Morton and his co-workers [5] have emphasized the cardioinhibitory function of the vagus on the sinoauricular node and a-V bundle and have pointed out that these effects are potentiated by the anoxic state. Burstein [6] and Harken [7] and their co-workers have also demonstrated the relationship of the vagus nerve to the development of cardiac arrhythmias.

Certainly, the slowing of the rhythmicity of the sinoauricular node and the shifting of the pacemaker to the a-V node can be explained by vagal efferent depressor effects. The further shift of the pacemaker to lower down in the a-V node with aberrant excitation and recovery (i. e., nodal rhythm, rate 75 per minute, with deeply inverted T wave) can be attributed to the additional factor of anoxia secondary to the apnea. Proper respiratory exchange and discontinuance of surgery until anoxia was corrected may have prevented cardiac standstill and ensured a successful outcome. In this respect, it is important to note the advantage to be gained from a team consisting of a surgeon, an anesthesiologist, and a cardiologist.

SUMMARY

The diagnosis and surgical repair of a partial eventration of the right hemidiaphragm in an infant with arthrogryposis are discussed.

Serratus anterior and latissimus dorsi musculature could not be demonstrated at operation.

Biopsy of the diaphragm failed to reveal any muscle abnormality, indicating that the eventration was coincidental and unrelated to the arthrogryposis.

Nodal rhythm and apnea were induced by traction on the diaphragm and mediastinum and presumably were caused by cardioinhibitor reflexes mediated throughout the vagus.

Prompt recognition and correction of apnea restored the regular sinus rhythm and prevented cardiac standstill.

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SUBMUCOSAL SALINE WHEAL AS SAFETY FACTOR IN FULGURATION OF RECTAL AND SIGMOIDAL POLYPI

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SURGICAL textbooks emphasize the need for care in the electrosurgical treatment of adenomatous polypi of the upper rectum and sigmoid colon, particularly when the lesion is on the anterior rectal wall or above the peritoneal reflection. In these areas, through-and-through coagulation of the colonic wall may lead to (1) injury to the vagina, in the female, or to the seminal vesicles or bladder, in the male; (2) delayed hemorrhage, when separation of too deep a slough uncovers a blood vessel of large size; (3) intestinal obstruction due to adhesion of a loop of small bowel to serosal exudate over a coagulated area,[1] or (4) peritonitis, when the necrotic area borders on peritoneum.

The true incidence of such complications is not known, and it is reasonable to assume that the occasional fatality, with the unfavorable stigma it attaches to the operating surgeon, is not always reported in the literature.

In the electrosurgical attack on rectal and sigmoidal polypi, four techniques are available:

(1) Fulguration, or the use of the monopolar (Oudin type) current, sparking across an air gap from electrode to lesion

(2) Electrodesiccation, or the employment of the monopolar current with the electrode in contact with the lesion

(3) Electrocoagulation, or the destruction of the lesion by cooking or by the thermal effect of a biterminal diathermy current

(4) The use of a snare or pedicle forceps for crushing the stalk of a pedunculated lesion with simultaneous application of a coagulating current through the instrument.

Monopolar fulguration is considered least likely to cause deep burning of the bowel wall, and the use of the diathermy snare with a biterminal coagulating current for pedunculated lesions seems to enjoy almost equal popularity in electrosurgical polypectomy.

Because of the variability in current intensity from one momentary application to another and because of the variability in the thickness of the colonic wall from patient to patient, and even in the same person the employment of all available safety factors seems warranted, especially if complete destruction of a lesion known to be precancerous is to be one's goal.

With the knowledge that the submucosa of the colon is made up of areolar tissue over which the mucosa is somewhat moveable, a study was begun to determine the ability of a saline wheal, injected through the mucosa into this layer, to protect the deeper layers of the bowel from thermal injury.

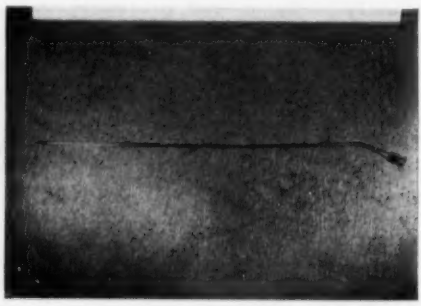

Fig. 1.—One type of 30 cm. 23-gauge needle for introduction of submucosal saline wheal through standard 25 cm. sigmoidoscope. A similarly designed needle, with tip in line with main axis of shaft, has also been employed. (The needle was specially constructed by Becton, Dickinson & Company, Rutherford, N. J.)

TECHNIQUE

The following in vitro experiments were carried out: A grossly normal-appearing segment of human sigmoid colon obtained soon after its operative removal was carefully trimmed of its external mesenteric and epiploic fat tissue. The bowel was opened longitudinally and all intraluminal con-

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tents flushed away with isotonic sodium chloride solution. The strip of bowel was then placed, mucosal side upwards, on an indifferent metal electrode connected to a portable Bovie Electrosurgical Unit.* This electrode consisted of a malleable metal plate measuring 16 by 6.5 cm. The spark gaps in the unit were standardized in accordance with the manufacturers' directions, and the coagulating current indicator was set arbitrarily at the "60" mark. A metal "ball" electrode, 4 mm. in diameter was employed as the active electrode, and it was held in light contact with the bowel mucosa during the coagulation.

wall were fixed in 10% formalin and subjected to microscopic examination, the section chosen being through the approximate center of the burned area. Hematoxylin and eosin as well as special stains were employed.

RESULTS

I. *Controls.*—A. Five-Second Burns: The mucosa was disorganized, with distorted "exploded" tubular glands and disappearance of interglandular connective tissue. Superficial mucosa charring was noted. In the sub-

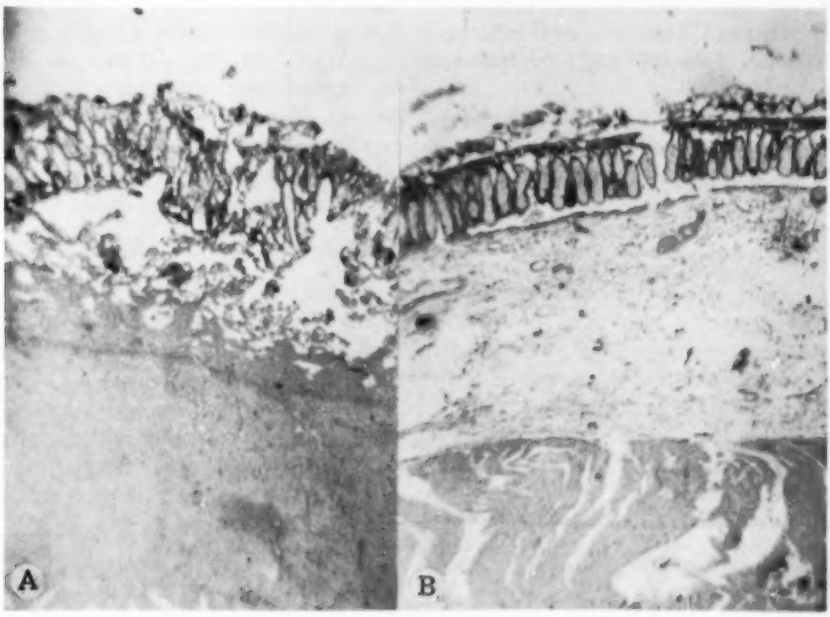

Fig. 2.—*A*, Five-second burn. Note extensive charring and distortion of mucosa, with vesicle-like spaces in submucosa. Zone of amorphous coagulation necrosis is present in deeper submucosa, also involving inner layer of muscularis. *B*, Five -second burn after production of submucosal saline bleb. Note widening of submucosa and looseness of submucosal connective tissue due to introduced saline solution. Note superficial charring of mucosa, without appreciable evidence of deep submucosal or muscularis coagulation.

Some control areas were subjected to continuous 5-second applications of the current, and some were treated for 10 seconds. In other portions of the colon, submucosal injections of 1 cc. of isotonic sodium chloride solution were made through a 23-gauge needle prior to electrocoagulation. The solution was easy to introduce into this loose tissue plane and formed an elevated wheal.

After completion of the experiment, blocks of tissue comprising the entire thickness of bowel

*Manufactured by the Liebel-Flarsheim Company, Cincinnati.

mucosa the collagenous tissue fibers were swollen and confluent in places and had a hyalinized, glassy appearance. The muscularis mucosa blended with, and was indistinguishable from, this layer. In some slides, the inner portion of the muscularis showed coagulative necrosis plus fine vacuolization.

B. Ten-Second Burns: The changes were similar to those described for five-second burns but were more marked. The area of

mucosal destruction was wider, and approximately seven-eighths of the inner circular layer of muscularis was coagulated.

II. *Saline Wheal Areas.*—A. Five-Second Burns: Mucosal damage was essentially similar to that seen in controls. Damage to submucosal connective tissue, however, seemed minimal, with connective tissue fibers dispersed and separated, apparently due to the saline solution injected into this layer. There were degenerative coagulation changes in the muscularis mucosa, but the tunica muscularis appeared normal. There was some minor focal lifting up of the epithelial layer from the muscularis mucosa.

B. Ten-Second Burns: Very little difference from results obtained in the five-second burns was noted.

COMMENT

The thickness of the bowel in the region of the rectosigmoid and lower sigmoid colon varies from one specimen to another and in different areas of the same specimen. Greater thickness is encountered in the region of the muscular teniae and in areas where the subserosal fat is great. The areas between the teniae are, however, devoid of the reinforcing outer longitudinal layer of muscle, and these areas are often devoid of appreciable subperitoneal fat. A specific current intensity may therefore be safe in one area of bowel and dangerous in another.

The relation of the in vitro observations made on normal freshly removed colon to the clinical treatment of polypi by electrocoagulation or fulguration is apparent. By temporarily increasing the thickness of the bowel wall at the site of the lesion, using a submucosal saline wheal for that purpose, a safety factor is introduced, and the chances of through-and-through destruction of colonic wall are diminished.

This method has been tried clinically in a small group of cases without ill effects. A long 23-gauge needle (Fig. 1), specially constructed for use through a 10 in. (25.4 cm.) sigmoidoscope has been employed. Sodium chloride solution was employed in each instance, although a weak solution of epinephrine might, through its vasoconstrictor effect, delay absorption of the wheal.

CONCLUSION

A saline wheal, introduced into the submucosa beneath a sigmoid or rectal polyp prior to electrocoagulation or fulguration of the lesion, may afford protection against too great a thermal injury to the bowel wall. The technique would seem particularly applicable to sessile polyps situated either on the anterior wall or above the peritoneal reflection.

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FAILURES WITH TANTALUM GAUZE IN VENTRAL HERNIA REPAIR

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DURING the last seven years 139 cases of large ventral hernias with poor tissues have been operated upon using tantalum gauze in the repair. In approximately half these cases the edges of the defect could not be approximated. In these cases, flaps of the sac, reinforced with whatever scar tissue was present, were first overlapped to close the defect, and then the entire area was covered with tantalum gauze. In the other half of the cases, in which the fascial edges of the defect could be approximated, tantalum gauze was used to reinforce the suture line, either because of the weakness of the surrounding fascia or because of the tension under which the edges were approximated. In the early cases only a small strip of tantalum gauze was used to reinforce such suture lines. In five of these cases there were so-called false recurrences; that is, a hernia occurred at the edge of the implanted piece of tantalum gauze, while the site of the original hernia remained firm. Apparently these "false recurrences" were due to entirely too small a piece of tantalum gauze being used to reinforce a suture line that was surrounded by weak fascia. The weakness of the fascia invited the occurrence of a hernia at the edge of the implanted tantalum, where the support of the weakened fascia stopped. Since the appearance of these "false recurrences," a piece of tantalum gauze large enough to reinforce the entire weakened area has been used. In several cases the entire abdominal wall has been reinforced with the material, using a piece 12 by 12 in. (30 by 30 cm.) in size.

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All the patients operated upon have been carefully followed each year, except for a very small number who have moved, leaving no address. I have recently reoperated in the first two cases of frank recurrence following the use of tantalum gauze in ventral hernias. I have also operated on an entirely different type of false recurrence from those mentioned previously. The experiences with these cases seem worth while reporting.

REPORT OF CASES

CASE 1.—L. R. E., a policeman, white, aged 59, was first seen by me on Oct. 13, 1952. The patient had had an operation for peptic ulcer in October, 1951. Three weeks after that operation he developed a hernia in the operative scar, which continued to get larger and which caused him considerable discomfort.

Physical Examination.—The patient was a large man, 6 ft. (183 cm.) tall, weighing 210 lb. (95 kg.). There was a midline operative scar extending from the xyphoid to the umbilicus. A huge hernia protruded throughout the entire extent of the scar. The fascial defect, which could be easily felt with the patient lying down, measured 8 in. (20 cm.) in length by 5 in. (13 cm.) in width.

Operation.—The patient was operated upon at the Church Home and Hospital on Nov. 3, 1952, under thiopental (Pentothal) sodium and nitrous oxide anesthesia. A long incision was made from well above the xyphoid to near the symphysis. The huge hernia sac was dissected free without opening it, and the fascia was cleaned well away from it in all directions. The sac, which was well reinforced with fibrous tissue, was then opened longitudinally and found to contain adherent omentum. The omentum was freed, and almost all of the greater omentum was resected in order to provide more intra-abdominal space. The flaps of reinforced hernia sac were then overlapped. The edge of the right flap was sutured to the fascial edge on the left side. Then the left flap was placed over the right flap and its edge sutured to the right fascial edge. Continuous sutures of No. 0 braided tantalum wire were used for suturing the flaps in place. Before the flaps were sutured, however, a relaxation incision had been made in the rectus sheath on each side, allowing the edges of the defect to be brought about 2 in. (5 cm.)

closer together than had been possible before the relaxation incisions were made. Even at that, the defect, which was covered only by two flaps of reinforced peritoneum, was very large. The entire area was reinforced by suturing over it two pieces of tantalum gauze, each 6 by 11 in. (15 by 28 cm.), using tantalum wire (0.01 in. in diameter) as suture material. These strips of gauze were placed parallel to each other and sutured together, with their edges overlapped in the middle. They covered not only the defect itself, but also the relaxation incisions in the sheath of the rectus muscle which had been made on each side of the defect. A stab wound was made in the lateralmost portion of each dissected skin flap, and a cigaret drain was placed through each stab wound. The subcutaneous tissue was closed with interrupted 0 plain absorbable surgical (gut) sutures; the skin was closed with continuous fine black nonabsorbable surgical (silk) sutures.

Postoperative Course.—Following operation, there was rather stubborn distention for a few days, and the patient developed an annoying cough. The drains were shortened on the third postoperative day and removed on the fifth postoperative day. On the 10th postoperative day it was noticed that there was considerable encapsulated fluid under the upper part of the incision just below the xyphoid; 200 cc. of blood-tinged fluid was aspirated. The same amount was aspirated two days later, and he was discharged from the hospital the same day.

On a visit to my office two days later, there was so much fluid that a small incision was made in the wound in order to allow it to drain. The drainage continued for another month and the wound became infected [1]. There was a persistent sinus tract, which refused to heal, and the tantalum gauge could be felt with a probe. By this time a recurrence of his hernia which was approximately half the size of the original hernia had developed.

On May 27, 1953, the sinus tract was explored with the patient under lidocaine (Xylocaine) infiltration anesthesia at The Johns Hopkins Hospital, as an outpatient. It was found that a buckled-up piece of tantalum gauze, about the size of a quarter, had not been infiltrated with the surrounding tissues. This was removed, cutting it back to where the gauze was thoroughly imbedded in the tissues. After removal of this, the wound healed promptly.

Second Operation.—Operation for the recurrent hernia was performed at the Church Home and Hospital on June 27, 1953, with the patient under thiopental (Pentothal) sodium, nitrous oxide, and ether anesthesia. A midline incision was made, excising the old scar. The subcutaneous tissue was dissected well away from the hernia. The tantalum gauze, infiltrated by fibrous tissue, was found to be intact, but the large hernial bulging included the tantalum gauze. The tantalum gauze, heavily reinforced by fibrous tissue which had grown through and around it, was opened in the midline, as was also the peritoneum. It was found that at the lower end of the defect there was a second sac, which was a lobule of the main sac, and which was about the size of an orange. This was repaired by pulling the sac into the peritoneal cavity, excising it, and closing the peritoneum from within. The peritoneum was then closed with a running suture of heavy black silk. The right flap of fascia-reinforced tantalum was then sutured to the left edge of the defect. The flap was weak in places and was therefore reinforced by suturing over it a piece of tantalum gauze 6 by 4½ in. (15 by 11 cm.). The left flap of fascia-reinforced tantalum gauze was then sutured over the right flap, but was only large enough to cover about half the right flap. Interrupted sutures of heavy black silk were used as suture material in reforming these flaps. In view of the trouble encountered from a postoperative collection of fluid at the previous operation, four stab wounds, instead of two, were placed in the skin flaps (two on each side), and a cigaret drain was placed through each of them. A Penrose drain was placed in the lower angle of the wound. The subcutaneous tissue was closed with interrupted medium black silk sutures; the skin, with interrupted vertical mattress sutures of fine black sik.

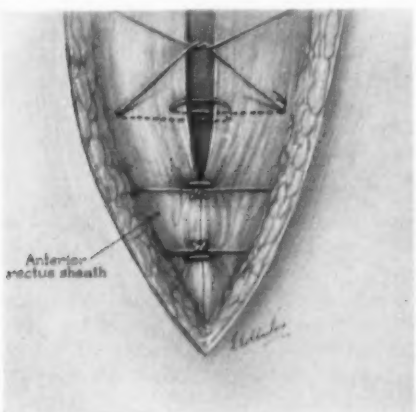
Postoperative Course.—The cigaret drains were left in a little longer than at the previous operation, and the patient's postoperative course was smooth. He was discharged from the hospital on the 10th postoperative day. The patient was last checked on Jan. 3, 1955. The hernia site was firm, and the patient was working every day at his job on the active police force of Baltimore.

Comment.—In the first place, I might state that, in my experience, large epigastric hernias are very difficult, probably the most difficult of all, hernias to cure. In the large ones the edges are widely separated and cannot be approximated except by some kind of plastic operation. If they are approximated, the tension is bound to be great because the rigidity of the rib cage does not allow any "give" in the environs of the hernial defect.

When I left the operating room after doing the second repair on the case here reported, one of my colleagues remarked to me in a jocular manner: "I see you are doing your hernias in two stages now." That is

exactly what did happen in this case. The first operation did not cure the hernia, but the implanted pieces of tantalum became so infiltrated with fibrous tissue and so strong that they furnished adequate flaps for effecting a cure at the "second stage" of the operation.[2]

Since operating on this case, I have operated on a similar case in which the "first stage" was done by another surgeon. At the "second-stage" operation I was able to fashion strong fascia-reinforced tantalum flaps, which could be overlapped, making a secure repair.



This drawing shows the type of traction suture used. The suture nicely approximates the fascial edges in cases in which there is some tension. It is also useful in cases in which there is no tension but in which the fascia is poor, and in which sutures in the fascial edges themselves are likely to pull out. The suture distributes the tension over a wide area of the fascial plane, instead of leaving it simply at the fascial edges. Heavy silk is used because it does not tend to cut through, as silk of a smaller caliber does. The notion that no suture should be used that is stronger than the structures sutured is fallacious in this respect. No matter how strong a small suture is, if it cuts through, it defeats its purpose. Between the tension sutures, interrupted sutures of a smaller-caliber silk are used. The traction suture is not original with me, but has been used widely in Baltimore for many years. I do not know who originated the suture.

There are several factors which contributed to the recurrence in this patient. Among them were his cough and distention. However, there is one very important lesson to be learned from it, and that is that the drainage was not sufficient; else he would not have had the enormous collection of fluid after the drains were removed. When such large pieces of tantalum gauze are implanted, four drains instead of two should be placed through the skin flaps, and they should be left in place long enough to make sure that the collection of fluid has ceased.

Recently,[3] a new method of draining these cases has been devised, consisting of four catheters, with multiple perforations, placed through four small stab wounds (two on each side) in the skin flaps and connected to a suction apparatus. This method keeps the wound absolutely dry. The catheters may be removed in three to five days without any danger of further collection of fluid.

CASE 2.—Mrs. M. E., a 43-year-old housewife, was first seen by me on Feb. 3, 1950. She had had six abdominal operations for various conditions, which eventuated in a huge incisional hernia, the size of a medium-sized watermelon. It could not be completely reduced even with the patient lying down. The patient was very obese, being 5 ft. 2 in. (157 cm.) tall and weighing 210 lb. (95 kg.).

Operation.—The patient was operated upon at the Church Home and Hospital on Feb. 28, 1950, under thiopental (Pentothal) sodium and ether anesthesia, with curare. A transverse incision was made midway between the umbilicus and the symphysis, going all the way across the abdomen. The huge hernia sac was dissected out and excised and the omentum and intestines reduced into the abdominal cavity, with some difficulty. The edges of the hernial orifice were sutured in a transverse direction under considerable tension. The suture line was reinforced with a piece of tantalum gauze. This was done, not only because the edges of the hernial defect had been sutured under tension but because the surrounding fascia was very weak.

Postoperative Course.—The patient did very well after operation. She was discharged from the hospital on the 11th postoperative day. She was observed at intervals until June 30, 1950, at which time the operative site was very firm. She returned, however, on Feb. 5, 1951, with a mass about the size of a hen's egg just to the left of the midline and below the old operative site. She gave a history of having had a terrific cough during the preceding couple of months.

Second Operation.—At this operation, on Feb. 27, 1951, it was found that the original operative site was firm but that a new hernia sac had appeared (one of the five so-called false recurrences mentioned above) below the piece of tantalum implanted at the first operation. This sac

was not opened, but simply inverted under transverse mattress sutures of heavy black silk. A large piece of tantalum was then implanted, covering the entire lower part of the abdomen, the lower border of the mesh being sutured to the symphysis pubis.

Postoperative Course.—The patient's convalescence was uneventful. She was discharged from the hospital on the 10th postoperative day. She was followed at frequent intervals, and every effort was made to get her to reduce her weight, all of which were unavailing. Toward the end of 1953, a weak spot developed in the center of the operative site, but no actual hernia could be made out. This was still true when she was examined on Feb. 1, 1954. However, on March 1, it was obvious that she had a hernia, and it was felt that the hernia had broken through the middle of the implanted tantalum gauze.

Third Operation.—This was performed on March 18 again through a long transverse incision. A lipectomy was first done. It was found that the hernia had broken all the way through the implant of tantalum gauze. The hernial defect measured 3 by 2 in. (7.5 by 5 cm.). The edges of the defect were very firm, consisting of fibrous-tissue-infiltrated tantalum gauze. These flaps were closed in a transverse direction with sutures of heavy black silk, interrupted. Flaps of fascia could be fashioned to reinforce the first suture line. The ultimate closure was very strong.

Postoperative Course.—Again the patient's postoperative course was entirely uneventful, and again she was discharged from the hospital on the 10th opstoperative day. She is now finally beginning to reduce her weight under the specific directions of a dietician. When last seen, on Sept. 29, her weight was down to 181 lb. (82 kg.), and the hernia site was very firm.

Comment.—I feel that the third operation in this patient would have been very difficult, and possibly impossible, had not tantalum gauze been implanted at the second operation in a large piece. This had become so thoroughly infiltrated with fibrous tissue as to furnish a very strong fibrous-tissue-reinforced tantalum sheet to use for closure. It is believed that this patient would not have had a recurrence if she could have been persuaded to reduce her weight. The average doctor will not take the time and trouble to outline a specific diet for patients, nor is he well enough trained in dietetics to do so. It is best to turn such patients over, early in the game, to a well-trained and hard-boiled dietitian.

Case 3.—M. T., a 46-year-old business man, was first seen by me on April 20, 1954. He had had a cholecystectomy in November, 1952, which was followed by a hernia. In January, 1953, and again in May, 1953, attempts were made to repair the hernia, both of which failed. When I first saw him, he had a huge bulging in an upper right rectus operative scar, and on lying down the defect measured 8 in. (20 cm.) long by 4 in. (10 cm.) wide.

Operation.—Operation was performed at The Johns Hopkins Hospital, with the patient under continuous spinal anesthesia, on April 22. After the hernia sac was dissected out and excised, relaxation incisions were made in the sheath of the rectus on each side of the hernial defect. The defect could be closed with traction sutures (Figure) of heavy braided silk. It was discovered, however, that the relaxation incision, which had been made to the left of the hernial defect, was in the midline and that at the upper end of the incision in the epigastric region there was no muscle under the incision in the fascia. An attempt was made to close the fascial edges, but the closure was under considerabe tension, and it was felt that the sutures might not hold. The entire area was covered with tantalum gauze.

Postoperative Course.—The patient's postoperative course was very stormy. He coughed a great deal, having a chronic lung infection. The abdomen also became markedly distended, in spite of the presence of a Levin tube. While his hernia site remained firm, it was obvious that he had a weak spot in the epigastrium where the relaxation incision had been made. He was discharged from the hospital on the 21st postoperative day.

He returned for observation on June 1, at which time it was obvious that he had a hernia in the epigastrium, and it was felt that this was due to a weakening in this area occasioned by the relaxation incision made in order to close the hernia in the gall bladder incision.

Second Operation.—This operation was performed on June 3, through a midline longitudinal incision from the xyphoid to below the umbilicus. An ellipse of skin was taken out at the time the incision was made, to be used as a cutis graft later, if necessary. The hernial defect measured approximately 2½ by 3 in. (6.3 by 7.5 cm.), and its long axis was in the long axis of the body. A relaxation incision was made in the sheath of the left rectus muscle, and this time there was good muscle under the entire relaxation incision. The fascial edges were closed, using traction sutures of No. 2 braided white silk. The edges

were approximated without difficulty and without tension. However, there was one spot in the relaxation incision in the left rectus sheath where the muscle fibers themselves separated, exposing the posterior sheath of the rectus. This defect was closed with a full-thickness skin graft, suturing the edges of the graft to the edges of the rectus sheath and placing the graft in under considerable tension. The entire area, including the skin graft, was then covered with a piece of tantalum gauze approximately 6 by 5 in. (15 by 12 cm.). Drainage was effected by No. 18 F. catheters placed through stab wounds in the skin flaps, which were to be attached to suction machines later.

Postoperative Course.—After this operation the patient's convalescence was entirely uneventful. There was no distention. His cough was kept under control. He was discharged from the hospital a week after operation and returned to his home in Tennessee.

Comment.—The lesson to be drawn from this case is that relaxation incisions cannot be made with impunity unless there is muscle under the incision in the fascia. Had I placed a cutis (skin) graft in the defect made by the relaxation incision at the time of the first operation, the patient probably would not have developed a hernia in that incision. Skin grafts work very well in such areas, and small skin grafts are readily excised from the operative area. Full-thickness skin grafts can be put in without danger of complications, provided they are sutured in without tension. A great deal of the time is thus saved and the use of a dermatome rendered unnecessary. It is quite possible that cutis grafts would perform the same function as tantalum gauze, but the difficulty is that in cases with large defects it is difficult to get large enough pieces of skin, while tantalum in large pieces is readily available.

SUMMARY

Three instructive cases are here reported. The first is that of a difficult epigastric hernia with a large defect in which there was a recurrence, due to several factors: cough, distention, inadequate drainage of the collected serum, and, finally, infection. At the second operation, flaps could be fashioned out of the fascia-infiltrated tantalum which had been implanted at the first operation. By overlapping these flaps the hernia was successfully repaired. This repair might be called a "second-stage" operation for epigastric hernia, the tantalum implanted at the first operation having become so strongly infiltrated with fibrous tissue as to furnish material for the second repair, which was not available at the time of the first one.

The second case was that of a recurrent ventral hernia in the lower abdomen in a very obese person. Repair was again effected by the use of strong flaps of material consisting of fibrous-tissue-infiltrated tantalum gauze which had been implanted at the previous operation.

The third case was that of a hernia occasioned by a relaxation incision made to aid in the cure of a twice-recurrent incisional hernia.

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CARCINOMA OF GALL BLADDER

Report of Fifty-Two Operative Cases and Résumé of the Literature

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RECENT advances in surgical techniques have resulted in marked reduction in the morbidity and mortality following surgery for chronic cholecystitis and cholelithiasis. In many clinics the mortality has been reduced below 0.5%. However, one complication still portends an eventual mortality approaching 100%, namely cancer of the gall bladder. The recent simultaneous appearance of three such cases has lead to this review, including the 52 operative cases of carcinoma of the gall bladder encountered at the Beth-El Hospital in the past 20 years.

INCIDENCE

The earliest descriptions of cancer of the gall bladder were by Stoll, in 1777,[88] and by Halle, in 1786.* Since then, over 2,000 cases have been reported, 1,700 of which were reviewed in surveying the more recent literature.

According to the United States Bureau of the Census, more than 10,000 of 150,000 annual cancer deaths are due to cancer of the liver and biliary passages. Cancer of the gall bladder accounts for about two-thirds of these, or 6,500 deaths yearly. Considering the incidence of carcinoma and the size of the organ, Steiner [87] estimates that the individual gall bladder cell has a greater propensity for malignant transformation than any other epithelial cell in the body, except those in the uterine cervix. In my series, a carcinoma of the gall bladder was found in 52 of 2,250 biliary tract operations, an incidence of 2.3%. Various authors have reported an incidence from less than 1% [5] to more than 8%,[36] with a mean incidence in all reports of 1.9%. In more than 300,000 autopsies carcinoma of the gall bladder was encountered in 0.43%, comprising 4% of cancer deaths and as high as 10% of cancer deaths in women.†

The average age in our patients was 59 years, as compared with an average of 49 years in the patients having surgery for benign biliary tract disease. Only two patients with carcinoma of the gall bladder were under the age of 50, the youngest being 37. Biering [8] reported a case in a 13-year-old girl, and Kaufmann [49] encountered carcinoma of the gall bladder in a woman aged 95. However, in the series reviewed, most cases occurred in the sixth decade, with an average of 59.3 years. Among my patients, females comprised 86% of those with benign biliary tract disease and 90% of those with carcinoma of the gall bladder. In the reports of cases of carcinoma, an average of 76% (45 to 95%) were in females.

ETIOLOGY

Most, if not all, gall bladders, the site of carcinoma, demonstrate chronic inflammatory changes, with or without calculi. These inflammatory changes appear to be of long standing. The majority of investigators agree that a normal gall bladder rarely is the site of primary carcinoma, but the specific role of cholecystitis and/or cholelithiasis remains to be assessed. In our cases, the occurrence of carcinoma of the gall bladder an average of 10 years later than benign biliary disease tends to imply the presence of such disease for a number of years prior to the appearance of carcinoma. Further correlation is noted in that females predominated in cases of cholecystitis and of cancer of the gall bladder. Gallstones were present in over 90% of our

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* Halle,[41] cited by Cooper.[21]

† References 17, 33, 42, 46, and 56.

cases of gall-bladder carcinoma. Stones were demonstrated in 41 of 52 cases and were absent in only 4. In 7 the presence or absence of stones was not noted. In one case with a concomitant cholecystoduodenal fistula the gallstones may have passed into the intestinal tract. In reported cases, stones have been found in from 41 [46] to 100% of patients, with a mean of 78%. The true incidence is probably higher, since those cases in which the presence or absence of stones has not been determined are included in the group without stones. The prior existence of cholecystitis is further indicated by 50% of our patients having had symptoms suggestive of biliary tract disease for more than two years before the carcinoma was detected.

Gallstones per se may be important in causing cancer, not only because of mechanical irritation and the concomitant inflammation but also because of the possible carcinogenic effects of constituents of bile and gallstones, which are chemically related to known carcinogens.[14] Ewing [29] describes "precancerous" changes observed in inflamed gall bladders consisting of villous outgrowths, deep crypts, and disordered epithelium which may invade the muscularis. Rabinovich and Kieffer [76] demonstrate an undifferentiated basal layer in the epithelium, continuously dividing to produce new epithelium. They postulate that carcinoma results from the irritant acting directly on these cells, metaplasia of the mature epithelium not being a factor in production of carcinoma. Benign cystadenomas and papillomas are not common and, except in rare instances, do not undergo malignant change.‡

A number of investigators have implanted numerous irritants and carcinogens in the gall bladders of guinea pigs, rats, mice, and rabbits. In some cases they reported production of primary carcinoma with metastases.§ However, none of the animals died from the effects of metastases. Burrows [16] and Desforges and co-workers [28] demonstrate that the liver metastases described by these authors are identical with the benign glandular proliferation and liver infiltration occurring in animals having foreign bodies implanted in the gall bladder.

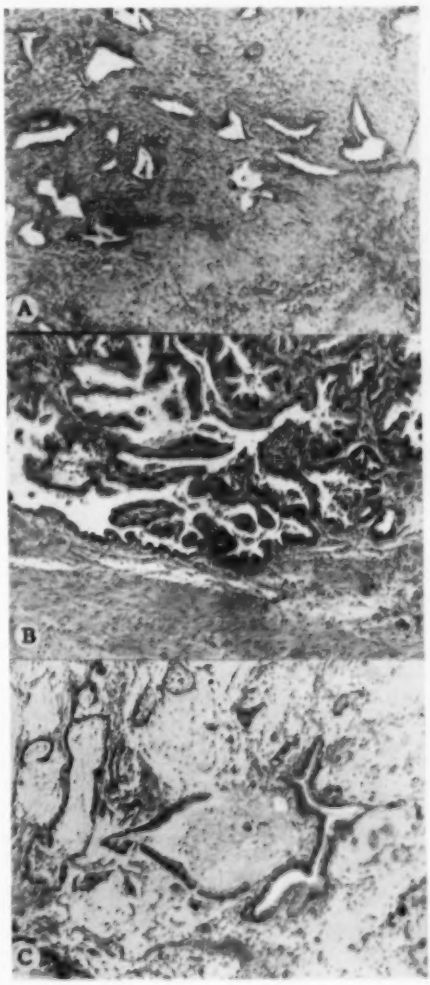


Fig. 1.—*A*, scirrhous carcinoma of the gall bladder; *B*, papillary adenocarcinoma growing into gall-bladder lumen; *C*, mucoid adenocarcinoma of the gall bladder.

PATHOLOGY

Carcinoma arises most commonly in the fundus or neck of the gall bladder.‖ The lesion is most commonly a scirrhous or med-

‡ References 10, 29, 44, 49, 66, 74, and 95.

§ References 50, 58, 63, 64, and 73.

‖ References 4, 29, 49, and 67.

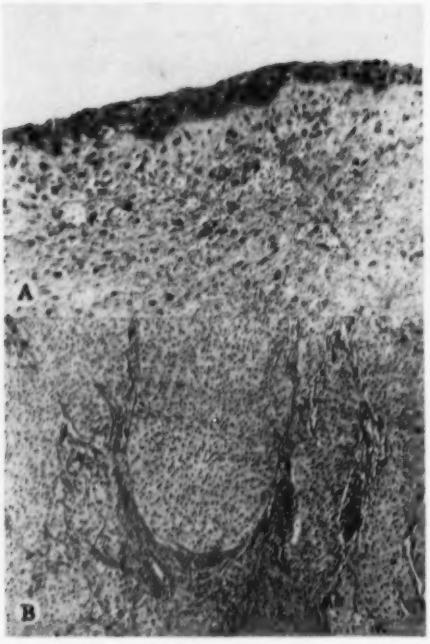
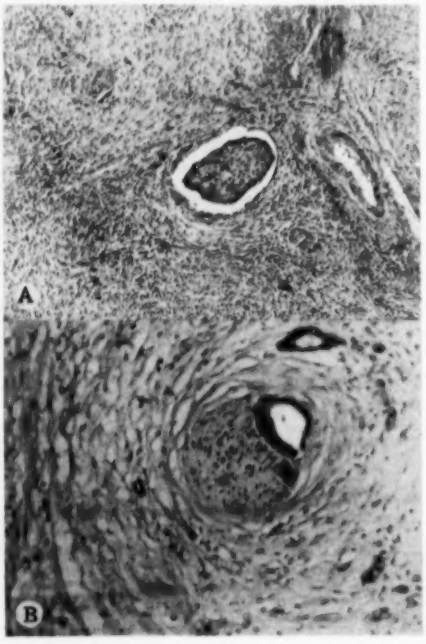


Fig. 2.—*A*, squamous metaplasia in gall-bladder epithelium. There is evidence of chronic cholecystitis. A squamous cell carcinoma was found elsewhere in this specimen. *B*, squamous cell carcinoma of the gall bladder.

ullary adenocarcinoma consisting of irregular cells or acini with a varying amount of interspersed fibrous tissue (Fig. 1*A*). This must be differentiated from "cystitis glandularis proliferans," a form of cholecystitis with glandular proliferation and invasion of the muscularis.[48] Grossly, the scirrhous carcinoma is seen as a hard, markedly thickened, contracted gall bladder, which can be mistaken for that of chronic cholecystitis. Less commonly, a papillary adenocarcinoma may occur (Fig. 1*B*). This frequently fills the gall-bladder lumen with a papilliferous tumor. These tumors may become very large and tend to adhere to adjacent organs, even before invading the liver. Degeneration of the tumor with hemorrhage within the gall-bladder lumen may produce acute symptoms.[18] Uncommonly, a mucoid adenocarcinoma is encountered, histologically characterized by large amounts of mucin and numerous signet cells (Fig. 1*C*). These tumors are very bulky and are prone to exhibit peritoneal metastases. In less than 10% of cases, squamous cell carcinomas are encountered. They may be fairly well differentiated, with frequent epithelial pearls demonstrable on histologic section (Fig. 2*B*). Normally, there is no stratified squamous epithelium in the gall bladder, but squamous metaplasia of the epithelium is frequently demonstrable in the presence of cholecystitis (Fig. 2*A*). Squamous cell carcinoma may arise directly from such metaplastic epithelium or from the undifferentiated basal cells. Squamous cell carcinoma grossly resembles scirrhous carcinoma.

In our series the medullary or scirrhous adenocarcinoma was encountered in 32 cases. Papillary adenocarcinoma was found in 10 cases, and there was 1 mucoid adenocarcinoma. There were four cases of squamous cell carcinoma and two cases of mixed squamous carcinoma and adenocarcinoma, the so-called adenoacanthoma.

Fig. 3.—*A*, squamous cell carcinoma in lymphatic vessel in gall-bladder wall; *B*, adenocarcinoma of the gall bladder invading perineural lymphatic and compressing the nerve.



The most important factors determining the virulent nature of carcinoma of the gall bladder are its anatomical location and its lymph drainage. The gall bladder has a rich lymphatic supply, consisting of intercommunicating submucous and subserous networks. By way of a common trunk, these drain into the cystic node at the junction of the cystic and common ducts, into the lymph nodes in the porta hepatis, and into those around the head of the pancreas. In addition, there are direct lymphatic connections between the gall bladder and the liver. Numerous lymphatics are also present around the autonomic nerves, supplying the gall bladder. Early lymphatic invasion (Fig. 3*A* and *B*) results in rapid spread along the course of the autonomic nerves and to lymph nodes that are surgically inaccessible. The tumor can also be expected rapidly to involve contiguous organs. Blood vessel invasion will also result in embolic spread to the liver. In addition to the liver, metastases from carcinoma of the gall bladder have been found in the adrenals, kidneys, pancreas, omentum, bone marrow, thyroid, and lung. To the latter, there may be direct spread via retroperitoneal lymphatics to the right lower lobe, without involvement of the liver.

SYMPTOMS

The symptoms are those to be expected considering the pathologic anatomy of the disease. Characteristically, the patient is a woman, past 50 years of age, with a history of gall bladder disease for more than 10 years. A few weeks or months prior to examination, the patient develops an exacerbation of her symptoms, with moderately severe unremitting right upper quadrant and epigastric pain. Early involvement of lymph nodes, resulting in jaundice, may occur. In addition, infiltration of the colon or duodenum may produce intestinal obstruction or fistulae to these organs.[46] On occasion, the disease may be heralded by an acute perforation of the gall bladder, with the symptoms of generalized peritonitis. On physical examination, a mass consisting of either tumor or an enlarged liver is palpable in the right upper quadrant of the abdomen. Unfortunately, all these are signs of advanced disease, early carcinoma of the gall bladder producing no symptoms other than those usually presented by the accompanying chronic cholecystitis and cholelithiasis.

Twenty-six (50%) of our patients presented a history suggestive of chronic biliary tract disease for from 2 to 32 years, with an average duration of symptoms of 11 years. In many patients there had been repeated attacks of biliary colic and previous roentgen demonstration of cholelithiasis. In one case gall stones had been noted as an incidental finding at laparotomy 10 years previously. In another patient cholecystostomy had been performed four years prior to the appearance of carcinoma. More careful interrogation of the remaining patients probably would have revealed an even higher percentage with long-standing biliary symptoms. It can be presumed that most of the remaining patients harbored "silent stones" until carcinoma developed.

Pain was the chief complaint in 47 cases. Of the 26 having biliary symptoms for more than two years, 22 had an exacerbation of pain one to five months prior to surgery. The severity and unremitting nature of the pain is probably due to tumor infiltration of perineural lymphatics in the gall-bladder wall (Fig. 3*B*). Jaundice was present in 35% of the cases. Four patients had painless jaundice, and three had choledocholithiasis; in two of them there was no tumor obstructing the common duct. An enlarged liver or mass in the right upper quadrant of the abdomen was palpable in 80% of cases. Most patients had evidence of recent weight loss, but anemia was not present in a significant number of cases. One patient appeared with an acute perforation of the gall bladder. Two others had had cholecystostomy for perforation of the gall bladder, carcinoma being detected when the cholecystostomy tract failed to close spontaneously. Two other patients had cholecystostomy for cholecystitis two or more years before carcinoma developed. One patient presented colonic obstruction from carcinomatous invasion of the he-

patic flexure. Four cases had cholecystoduodenal fistulae, and there were four instances of large liver abscesses secondary to tumor invasion. Most reported cases present a similar clinical picture. Many reports indicate a 50 to 80% incidence of cases with long-standing histories of cholecystitis prior to the development of carcinoma.¶

TREATMENT AND PROGNOSIS

Surgical therapy in the majority of cases of carcinoma of the gall bladder is palliative and of little avail. The usual case presents itself after lymph node or liver invasion is grossly in evidence. In 25 of my cases only biopsy or cholecystostomy was possible, the latter procedure being of doubtful value. Cholecystectomy was done in 27 cases. In 14 of these, concomitant choledochostomy was performed as a palliative procedure in the presence of unresectable metastatic tumor. Thirteen cases had resection of all grossly visible tumor, the lesion being extensive in nine of these. In the remaining four cases, the presence of carcinoma was grossly unsuspected by the surgeon, carcinoma being detected only after careful microscopic examination of tissue sections. These four cases should be expected to have the best therapeutic results. However, one patient died 22 months after surgery. One case was last seen with a large abdominal tumor mass, eight months postoperatively. A third woman, with a small, well-differentiated papillary adenocarcinoma, required hepaticoduodenostomy for obstructive jaundice due to tumor invasion of the porta hepatis, 26 months after initial cholecystectomy. Jaundice recurred nine months after hepaticoduodenostomy. One patient is living and well 40 months after cholecystectomy.

Z. G., a 55-year-old white woman was admitted on Feb. 28, 1950, with a 10-year history of biliary colic. Symptoms became more severe four months prior to admission. Examination revealed tenderness in the right upper quadrant of the abdomen, with no mass palpable. Surgery consisted of cholecystectomy, choledochostomy, and closure of a cholecystoduodenal fistula. Examination of the gall bladder revealed evidence of chronic cholecystitis, a small, fairly well differentiated papillary adenocarcinoma, and no calculi. The patient had an uneventful postoperative course. As of September, 1953, the patient was living and well.

This is our only patient still living and free of recurrence. Of 52 cases, 49 were traced. The remaining three had metastases at the time of surgery and are presumed dead. Fifteen patients died in the hospital, an operative mortality of 29%. Excluding the four cases in which carcinoma was an accidental finding on examination of the specimen, the average survival of patients leaving the hospital was 4.9 months, with only two patients living longer than 9 months. This is comparable to an average survival of 3.4 months reported by Sainburg and Garlock.[51] Most authors report cures in 0 to 5% of operative cases. In a group of 185 cases collected from the literature 7 were five-year survivors (3.6%) after surgery for carcinoma of the gall bladder.

When carcinoma of the gall bladder is encountered at surgery, resection of the gall bladder, a wedge of contiguous liver, and enlarged lymph nodes should be performed. All gall bladders removed for cholelithiasis should be opened at the operating table.[45] Any area suspected of being carcinoma is examined by frozen section, and if carcinoma is demonstrated, a lymph node and liver dissection should be performed. A rare case with lymph node or liver involvement may be cured by wide excision. Booker and Pack [11] report an eight-year survival following cholecystectomy, partial hepatectomy, and excision of two tumor-containing lymph nodes in a case of carcinoma of the gall bladder. Sheinfeld [53] reports moderate palliation with increase in survival time in a series of patients, with advanced gall-bladder carcinoma, undergoing cholecystectomy and partial hepatectomy.

COMMENT

The only effective means of combating cancer of the gall bladder is prevention. Carcinoma of the gall bladder is usually preceded by chronic cholecystitis and cholelithiasis.

¶ References 3, 10, 32, 41, 42, and 55.

Accordingly, whenever feasible, cholecystectomy should be performed on all patients in whom the diagnosis of cholecystitis or cholelithiasis is established.# This is justified not only because of the real danger of the appearance of carcinoma but also because of the probability of development of the other complications of chronic cholecystitis, i. e., infection, perforation, scarring, and choledocholithiasis, resulting in technically more difficult operation, with resultant higher morbidity and mortality. Since about 50% of patients with "silent stones" develop symptoms,* these cases should not be differentiated from the symptomatic group. The results of treatment of biliary disease can best be improved by discouraging the nonsurgical treatment of cholelithiasis.

SUMMARY

Fifty-two operative cases of carcinoma of the gall bladder are presented, with a review of the literature. Only one patient is living and well 40 months after surgery. The average survival of fatal cases was 4.9 months.

Cholecystectomy for "silent stones" is advocated to prevent carcinoma and other complications incident to cholecystitis and cholelithiasis.

Mr. Carl Erhardt, Director of the Bureau of Records, New York City Department of Health, gave assistance in tracing the patients. Mr. Rudolph Kurlen supplied the photomicrographs.

References 2, 10, 13, 21, 32, 35, 36, and 62.

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PSEUDOTUMOR OF CECUM

A Postappendectomy Finding

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THE CLINICAL and roentgenological significance of deformities of the cecum due to various operative procedures has not been given much consideration as evidenced by the few reports found in the literature. This report is concerned with the deformity produced by the inverted appendiceal stump and the problem of differential diagnosis of polypoid filling defects of the cecum.

The inverted stump of the vermiform appendix may persist for some time as a bulbous mass protruding into the cecal lumen and may appear in the roentgenologic examination as a small, rounded, or ovoid intraluminal filling defect at the usual site of the base of the appendix.* Artner,[1] in 1929, and Malbin,[6] in 1947, performing postmortem appendectomies on autopsy specimens, were able to reveal polypoid lesions in the cecum by means of barium x-ray studies and showed these x-ray findings to be due to the inverted stumps of the appendices. Artner further demonstrated that more than one-third of inverted appendiceal stumps are persistent and, in following a group of postappendectomy patients by means of barium enemas, he demonstrated that 8% of cases exhibited a "ring shadow" filling defect in the cecum regardless of the lapse of time since surgery.

Yeager,[10] Hayes,[4] and others have pointed out that the usual inversion of an appendiceal stump is not actually an inversion but is in reality a burying of the stump in a small blind pouch created by the inverting suture. Figure 1 is a representation of various methods of treating the appendiceal stump and shows the physical factors involved which may be capable of producing filling defects in the cecum in the postappendectomy patient. It would seem that similar cecal filling defects may be produced by inversion with or without ligature, the size of the filling defect being proportional to the size of the blind pouch produced by the inverting suture. The relative merits of methods of treating the appendiceal stump, however, need not concern us here.

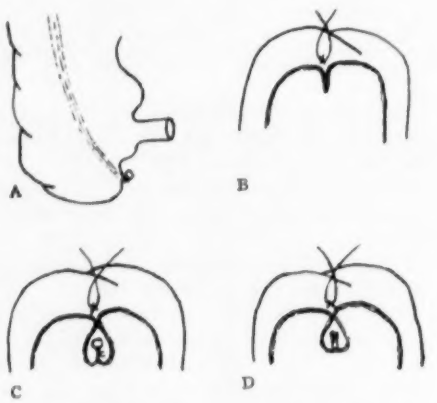

Fig. 1.—Schematic representation of various methods of treating the appendiceal stump: *A*, simple ligation; *B*, original Dawborn technique—true invagination into lumen of cecum; *C*, inversion and ligature; *D*, inversion without ligature.

The inverted stump of the appendix is generally considered to be innocuous except for the possibility that it may harbor an abscess. Schrager [7] has reported a case in which a

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* References 2, 3, and 8.

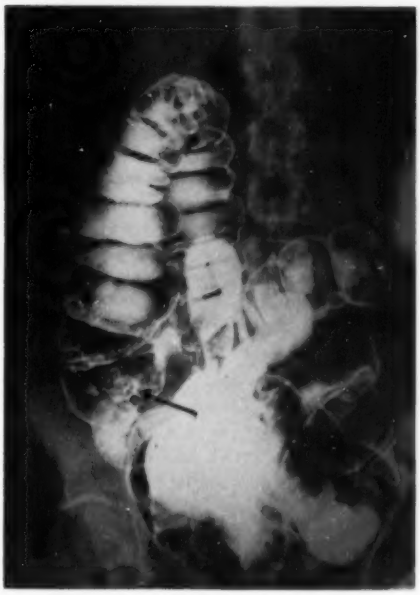


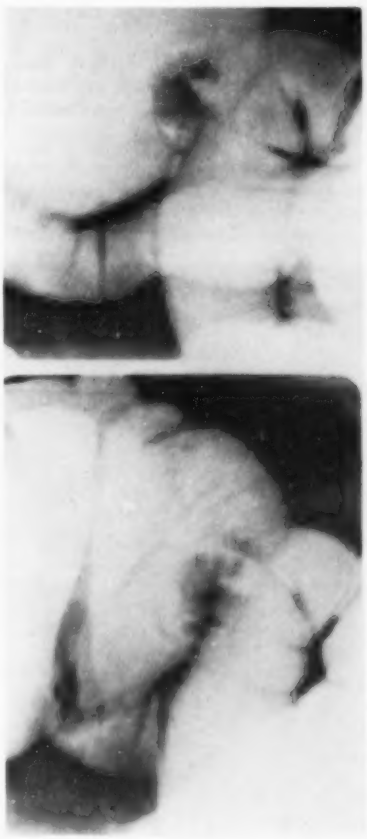
Fig. 2.—Roentgenogram of the colon made with double contrast method. The polypoid lesion in the cecum shown by the arrow proved at operation to be an invaginated appendiceal stump.

stump abscess lay dormant two years and then perforated into the general peritoneal cavity. Lowman and Mendillo [5] and Weber and Good [9] have postulated that the inverted stump might give rise to an intussusception. However, a more important consideration of this condition is one of diagnosis. Polypoid neoplastic lesions can and do produce similar roentgen defects in this area. True polyps with few exceptions are adenomas and should be eradicated, because of their marked tendency to undergo malignant degeneration.

There are no absolute criteria which will satisfactorily differentiate between the polypoid intraluminal defects produced by a persistent invaginated appendiceal stump and those produced by a polypoid cecal neoplasm.† In doubtful cases, barium enemas with air contrast studies should be repeated at frequent intervals. Any change in the size of the lesion and, more important, the presence of occult or gross blood in the stool should be an indication for surgical exploration.

Figures 2 and 3 are barium enema x-ray studies of a 47-year-old white woman who presented herself with complaints of chronic back pain. She had no definite symptoms referable to the colon. Past history revealed that she had undergone an appendectomy three years previously. Stool specimens were negative for blood, and the hemogram was normal. X-ray studies of the colon were repeated, revealing a constant filling defect of the

Fig. 3.—Spot compression films made of the barium-filled cecum, demonstrating the polypoid mass in the cecum arising from the medial wall and representing the invaginated appendiceal stump. Same case as represented by Figure 2.



† Ivie, J. McK.: Personal communication to the authors.

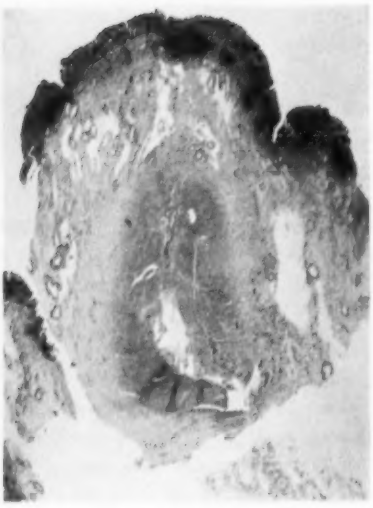


Fig. 4.—Photomicrograph of invaginated appendiceal stump showing the U-shaped invagination of mucosa and muscular walls of the cecum.

cecum. Since doubt existed as to the true nature of the cecal defect, exploration was advised. The colon was prepared with succinylsulfathiazole (Sulfasuxidine) and saline catharsis, and laparotomy was carried out. The cecum was found to be mobile, and a small, somewhat pedunculated, indurated mass was palpable at the junction of the taeniae coli on the medial wall of the cecum. The mesenteric lymph nodes did not appear unusual. Wedge excision of the involved area of the cecum was accomplished, revealing a firm polypoid lesion at the site of the previously removed appendix. Pathological diagnosis was returned as inverted appendiceal stump. Figure 4 is a photomicrograph of the specimen. Postoperative convalescence was uneventful, although the backache complaints remained unchanged.

Fig. 5.—Roentgenogram of colon made with double contrast method. The polypoid lesion in the cecum shown by the arrow proved at operation to be a benign adenomatous polyp.

Figure 5 represents barium enema x-ray studies on a second patient, whose cecal filling defect was found during the course of a general medical work-up. There were no specific symptoms referable to the large bowel, and, although there was a mild secondary anemia, no blood could be demonstrated in the stools. This patient, likewise, had previously undergone an appendectomy. Clinical and roentgenological opinions favored a diagnosis of cecal polyp, but the possibility of an inverted appendiceal stump was entertained. After preoperative preparation of the colon, a wedge resection of the involved medial cecal wall area was carried out. There was no semblance of an appendiceal stump to be found. Pathological diagnosis of the resected specimen was returned as benign adenomatous polyp of the cecum.

SUMMARY

The polypoid filling defect of the cecum which may follow appendectomy has been discussed. Two cases which exhibited similar clinical and roentgenological findings have been presented in order to illustrate the difficulty of differential diagnosis in polypoid filling defects of the cecum.

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NONRESPIRATORY POSTOPERATIVE SUBCUTANEOUS EMPHYSEMA

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POSTOPERATIVE subcutaneous emphysema has been reported by numerous authors. Usually it is associated with a defect in the respiratory system, and it is often a complication of general anesthesia.[1] One of two mechanisms usually is involved. When concomitant wounds occur in the parietal pleura, visceral pleura, and lung, air will pass from the injured lung across the pleural space with or without pneumothorax being apparent on roentgenograms during the early stages. The other mechanism which may be involved is the rupture of overdistended alveoli as a result of overinflation of the lungs, resuscitative measures, atelectasis with compensatory emphysema, or straining. Air bubbles escaping from the alveoli into the perivascular sheaths of capillaries and larger blood vessels coalesce and are pushed throughout the lung substance and down the lung root into the mediastinum. There are three main routes of egress from the mediastinum: the subcutaneous tissues of the neck, the pleural cavities, and the retroperitoneal space.[2]

Injury or ulceration of any part of the respiratory or gastrointestinal tract may permit the entry of air into the areolar tissue with migration to the subcutaneous tissue. Subcutaneous emphysema may be caused by sneezing or by energetic nose blowing. It may follow tonsillectomy, extraction of teeth, fractures of the paranasal sinuses, or any operative or accidental wound of the mucus membranes of the mouth, nose, or throat. Sechzer [3] reported a case of subcutaneous emphysema following cholecystectomy in which the site of entry of the subcutaneous gas was a pharyngeal ulcer and the driving force was the high pharyngeal pressure developed during strain and coughing while emerging from general anesthesia. Spontaneous rupture of the esophagus with mediastinal and subcutaneous emphysema has been recorded. Crepitation from air entrapped about wounds is seen commonly, especially in thin persons. Gas formed by bacteria also can cause subcutaneous emphysema.

Reports of subcutaneous emphysema originating from abdominal sources have not been frequent. Several instances of preoperative subcutaneous emphysema accompanying perforated peptic ulcer have been reported by Mc Corkle and Stevenson.[4] The authors suggested two mechanisms by which this could occur with an intact peritoneum: 1. A direct diffusion through the peritoneum. In a large series of therapeutic pneumoperitoneums done in tuberculosis patients under the care of Dr. John Middleton, at the University of Texas, Medical Branch, subcutaneous emphysema occasionally has occurred when large amounts of air have been used, but this has been more marked or localized to the site of the needle puncture and was felt to be due to slipping of the needle out of the peritoneal cavity or leakage through the puncture site. 2. A diffusion of gas from the site of perforation by subserous routes along peritoneum-covered ligaments about the stomach and duodenum and thence to the neck by way of the mediastinum, to the umbilical region by way of the round ligament, or to the retroperitoneal aveolar tissue and then around the abdominal wall or up the mediastinum to the neck.

Rankin and Judd [5] reported subcutaneous emphysema of the scrotum resulting from the perforation of a sigmoid diverticulum. Subcutaneous emphysema has been described resulting from gas formed by bacteria in peri-

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tonitis. Brown and Hinton [6] have recorded three cases of generalized subcutaneous emphysema secondary to leaking suture lines after colon surgery.

The following case of generalized emphysema is of interest.

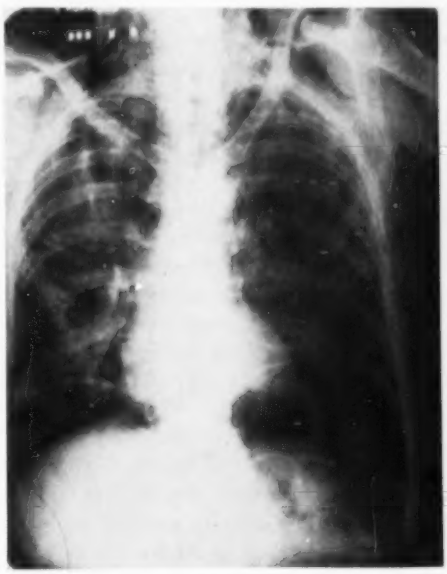
D. R. (Case 958 K), a 55-year-old white man, gave a history of recurrent pain typical of peptic ulcer over 20 years. He stated that he had been operated upon for an acute perforation of a gastric ulcer in 1947 and that hematemesis had occurred in 1953. He was treated medically with a Sippy diet, antiacids, antispasmodics and methantheline (Banthine) bromide, but medical management failed. He was referred from the medical to the surgical service for operation.

Examination at the time of admission revealed a malnourished man, alert and cooperative. Blood pressure was 120/60. Examination of the abdomen revealed an old right paramedian scar with a 3 cm. incisional hernia in its midportion. There was slight tenderness to deep palpation in the epigastrium and right hypochondrium. Rectal examination was negative.

Blood cell count, urinalysis, prothrombin time, blood glucose, nonprotein nitrogen, and serum protein determinations were normal. Roentgenographic studies of the upper gastrointestinal tract were interpreted as showing a diverticulum at the lesser curvature of the stomach adjacent to the cardia and an active ulcer on the lesser curvature in the prepyloric area. The chest roentgenogram was negative. Gastric analysis with histamine showed free HCl in all specimens.

On March 19, 1954, the patient was operated upon, with use of a transverse epigastric incision. A diverticulum was found on the posterior wall near the cardia, and a gastric ulcer was seen low on the lesser curvature. The diverticulum was resected; the resulting defect was closed, and a subtotal gastrectomy was done. The operative course was uneventful, and the patient returned to the ward in good condition. On the ward the administration of oxygen was started immediately by nasal catheter. Shortly thereafter the patient's abdomen became markedly distended, and a severe subcutaneous emphysema developed to involve the scrotum, the entire abdominal wall, and the subcutaneous tissue of the chest, neck, and face to the supraorbital level. The patient went into shock. The nasal oxygen tube was withdrawn and was found to have been inserted 5 cm. more distally than customarily recommended. Emergency roentgenograms of the abdomen revealed an extensive pneumoperitoneum. A presumptive diagnosis of perforation at the gastrojejunostomy suture line was made. After infusions of blood and electrolyte solutions the blood pressure, pulse rate, and respiration rate became stable, and the abdomen was explored. A perforation of the stomach was found at the site of closure of the diverticulum. This defect was closed. Within 24 hours after operation the subcutaneous emphysema had subsided almost completely. The postoperative course thereafter was entirely uneventful. The wound healed per primam, and the patient was discharged on the ninth postoperative day.

Though not recorded in the literature, several cases in other hospitals have been brought to our attention, in which a disastrous result followed when an oxygen cylinder was connected by error to the gastric suction tube instead of to the nasal catheter. As far as could be determined, this mistake had not been made in the case here reported.



Case 985 K. Film taken after operation showing extensive subcutaneous emphysema and pneumoperitoneum.

The next question which arose was whether an intranasal tube, even if introduced into the esophagus or too far into the pharynx, could cause the extreme gastric inflation which must have occurred in this case. To study this possibility the following experiments were carried out under local anesthesia in rabbits. Right rectus and transverse incisions were made in the abdominal

wall in separate animals and were closed in layers with sutures of 00 chromic absorbable (gut) sutures. Interrupted fine nonabsorbable surgical (silk) sutures were used for the skin. A needle was then introduced into the peritoneal cavity, and, by means of a large syringe fitted with a three-way stopcock, measured amounts of oxygen at atmospheric pressure were introduced. In cases in which the abdomen wall had been closed tightly with a continuous suture no emphysema resulted, although a pneumoperitoneum up to 1,600 cc. in volume was produced. In contrast, in cases in which the wall was closed loosely with interrupted sutures, generalized subcutaneous emphysema resulted when the intraperitoneal injection approximated 1,000 cc. in volume.

In other animals the abdominal wall was opened, with use of pentobarbital (Nembutal) sodium anesthesia, and the stomach was observed. A small plastic nasal catheter was then passed into the nostril of the rabbit, and oxygen was allowed to flow through the tube at the approximate rate of 6 liters per minute. When the tube had been introduced about 1 in. (2.5 cm.) into the nostril, the stomach began to distend; as the tube was passed distally the rapidity of inflation increased. The maximum rate of inflation occurred with the tube in the upper esophagus.

Insofar as such results in rabbits can be applied to human subjects, one must conclude that when a nasal oxygen tube is introduced too far into the pharynx, or when the mouth and contralateral nostril are obstructed, insufflation of the gastrointestinal tract may result from oxygen administration, and overdistention leading to rupture of suture lines can occur.

In summary, the case reported and the corollary animal experiments illustrate the potential danger of improper administration of intranasal oxygen. Care should be exercised in placing the nasal catheter when oxygen is given by that method. The tube must not be inserted too far distally, and a good airway must be maintained.

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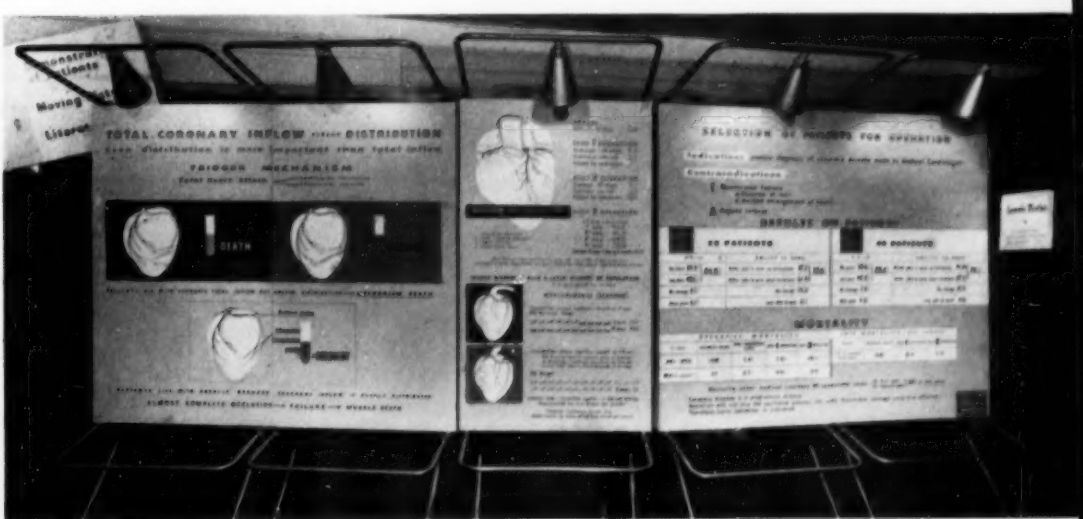
Scientific Exhibits

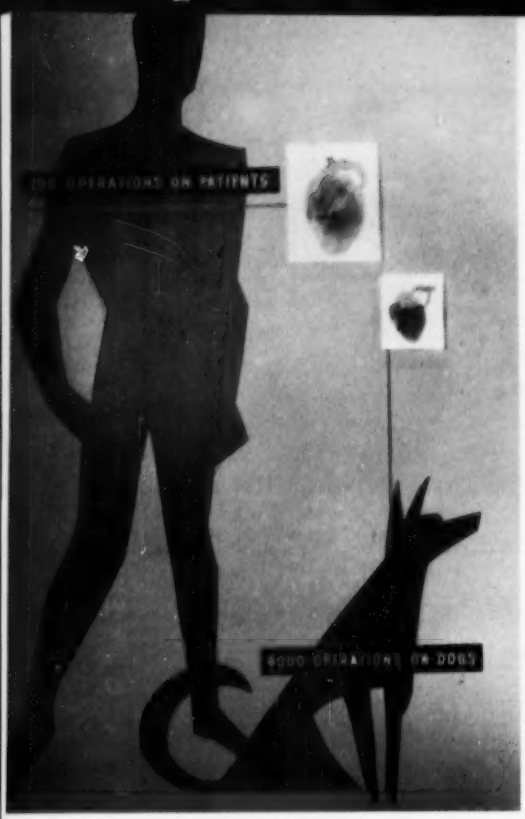
OPERATIONS FOR CORONARY ARTERY DISEASE

CLAUDE S. BECK, M.D.
AND
DAVID S. LEIGHNINGER, M.D.
CLEVELAND

DURING the past 20 years, approximately 4,000 experimental operations were carried out in the laboratory of Dr. Claude S. Beck on the coronary blood supply in dogs. The coronary vessels were dealt with directly, yielding information that could not be obtained in any other way. This experimental work made it possible to establish certain facts. Two operations for coronary artery disease, the Beck I and Beck II, are based upon these facts. The human figure symbolizes over 186 patients with coronary disease that have been operated on. To the right of the figure is a human heart embedded in plastic. A Beck II operation had been performed on the heart. The dog drawing symbolizes over 4,000 dogs operated on in the experimental laboratory. Above the drawing is a dog heart embedded in plastic. A Beck II operation had been performed on the heart.

Shown as a scientific exhibit of the Section on Surgery, General and Abdominal at the 103rd Annual Meeting of the American Medical Association, San Francisco, June 21-25, 1954. This exhibit was paid for by Thompson Products, Inc., Cleveland. The experimental work was supported by the U. S. Public Health Service and the Cleveland Area Heart Society.





PROBLEM: RED BLOOD TO HEART

The fundamental problem in coronary artery disease, other than prevention, is an inadequate blood supply to the myocardium. Treatment should consist of methods which can improve the blood supply to the myocardium.

How

1. EVEN DISTRIBUTION

INTERCORONARY COMMUNICATIONS (PERMANENT)

Fig. 1.—Normal dog heart: The descending coronary artery was injected with thick barium-gelatin solution. The solution will not go through a capillary bed. There was no filling of the circumflex artery. Normally there are few or no intercoronary arterial communications.

Fig. 2.—Dog heart: Beck I operation. Five weeks later, the descending and right coronary arteries were injected. Intercoronary arterial communications between the descending and the right coronary artery were filled. Intercoronary communications between secondary branches of the arteries are also filled with the injection mass.

Fig. 3.—Dog heart: Beck II operation. Five weeks after the second stage, the right and circumflex arteries were injected. The descending ramus was not injected. The descending artery was filled by way of intercoronaries.

2. ADDITIONAL BLOOD

(*a*) RETROGRADE FLOW IN VEINS (TEMPORARY—TWO MONTHS)

Arterialization of the coronary sinus by the Beck II operation provides additional blood by retrograde flow in the veins to the capillary bed where the arterial blood gives up its oxygen.

Fig. 4.—*A*, human heart: Beck II. Before reversal of flow. Vein graft between aorta and coronary sinus. Sinus not ligated. The veins were blue.

B, same heart, after reversal. The sinus was temporarily occluded to demonstrate reversal of flow in the veins. The veins were red.

C, dog heart: Beck II. Before reversal of flow. Vein graft placed between aorta and coronary sinus. Sinus not occluded. The arteries were red. The vein were blue.

D, same heart. After reversal. The sinus was ligated near its ostium. The left common coronary artery was completely ligated. The arteries were blue. The veins were red. There was complete reversal of blood flow in these vessels.

(*b*) EXTRACORONARY COMMUNICATIONS

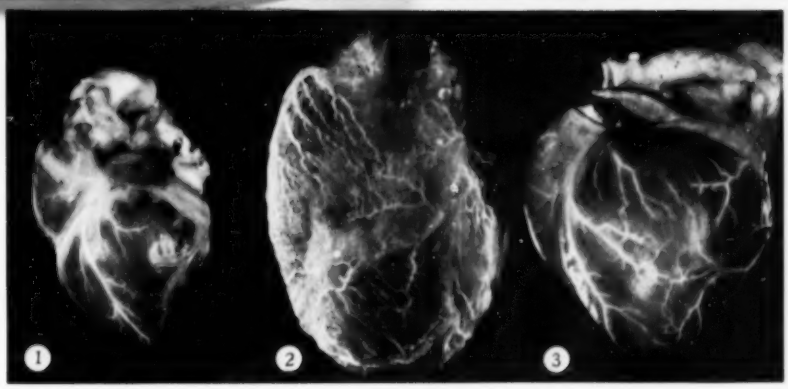
By grafting of tissue to the surface of the heart new blood vessels may grow across into the myocardium. This mechanism is inconstant.

Fig. 5.—Dog heart: Beck I. Omental graft. After operation the coronary arteries were injected. Vessels in the omentum filled with the injection mass. There were anatomical connections between the vessels in the graft and the coronary arteries.

Fig. 6.—Dog heart: Beck I. Pericardial graft. Five weeks after operation the coronary arteries were injected. Vessels on the surface of the pericardium and in the mediastinal tissue were filled.

3. ELEVATION OF SINUS PRESSURE (NOT ILLUSTRATED)

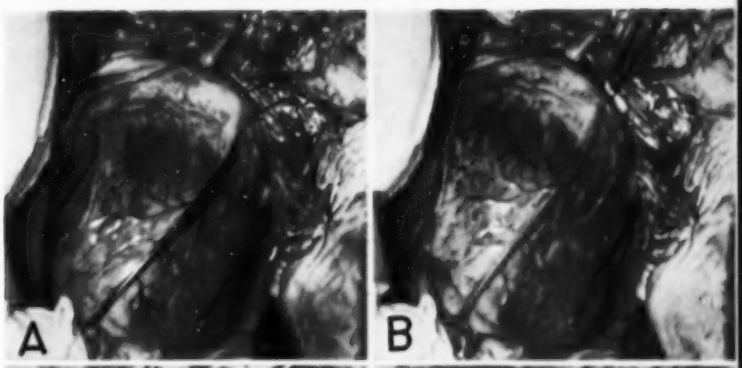
Elevation of the coronary sinus pressure by either arterialization of the sinus or by sinus ligation protects the heart against the effects of coronary artery occlusion.



How

1. Even Distribution Intercoronary Communications (permanent)

2. Additional Blood
(*a*) Retrograde flow in veins (temporary—2 months)



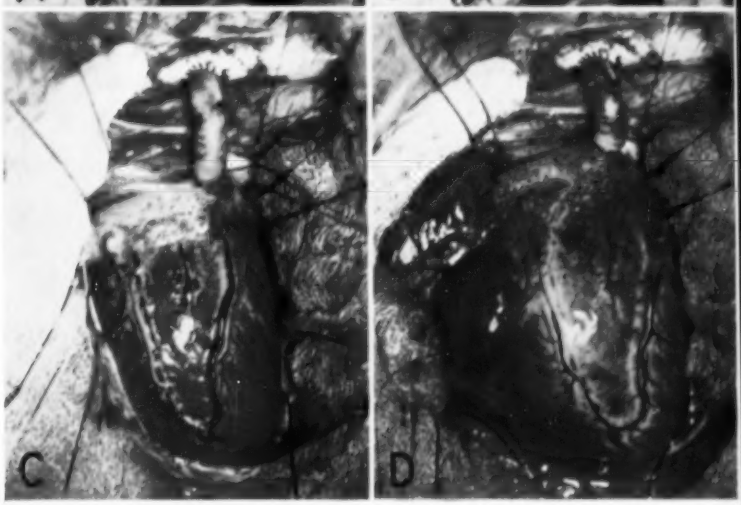
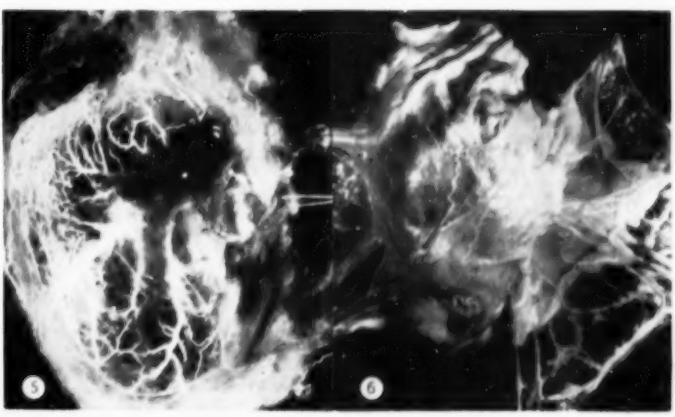
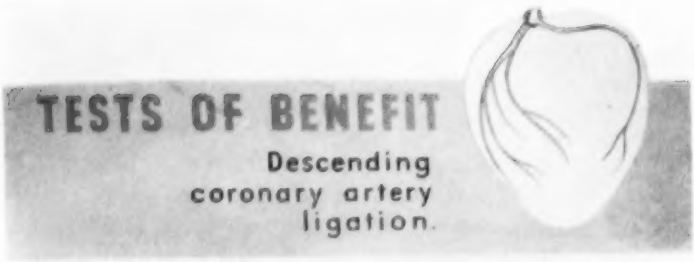


Figure 4



(*b*) Extracoronary communications

3. Elevation of Sinus Pressure (not illustrated)



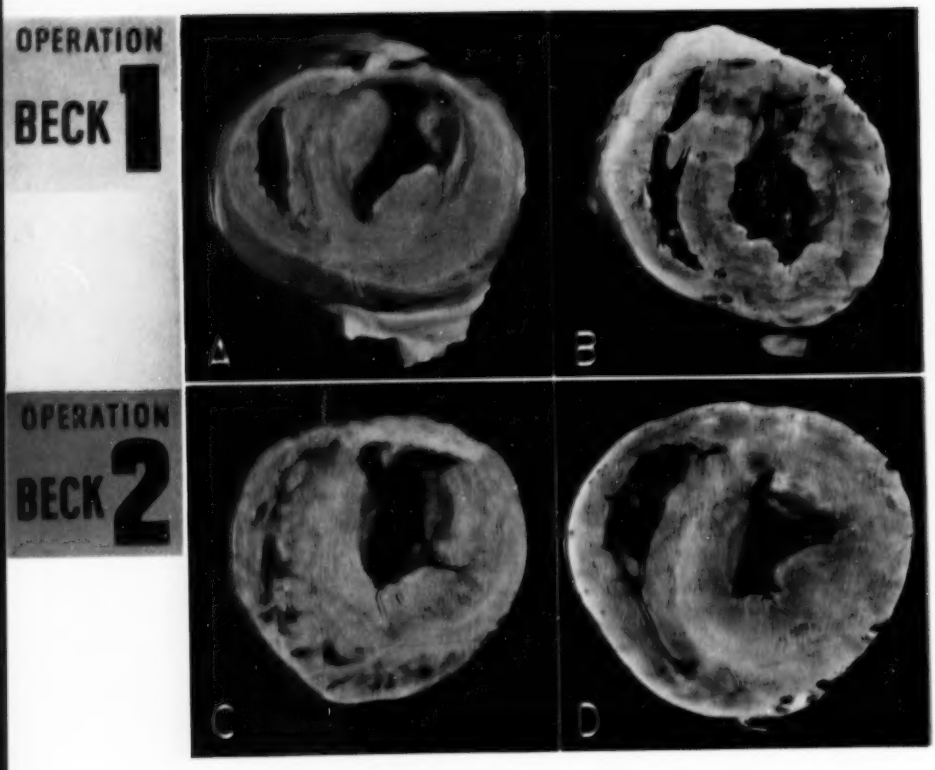


Fig. 7.—*A*, Dog heart: normal. Descending coronary artery ligated. The large infarct was typical of those found in the hearts of surviving control dogs.

Fig. 7 *C*.—Dog heart: normal. Descending coronary artery ligated. The large infarct was typical of those found in the hearts of surviving control dogs. Operation saved myocardium from destruction.

Fig. 7.—*B*, dog heart: Beck I. Circumflex coronary artery ligated. The cross section of the heart reveals a very small infarct. This infarct was typical of those found in the hearts of surviving animals. Operation saved myocardium from destruction.

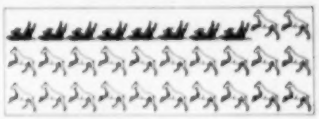
Fig. 7 *D*.—Dog heart: Beck II. Circumflex coronary artery ligated. The cross section of the heart reveals no gross evidence of an infarct. This was typical of many of the hearts of the surviving dogs. In some hearts a very small infarct was found similar to that found in Fig. 7 *B*.

The above drawing shows ligation of the descending ramus of the left coronary artery at its origin. The test compares mortality following artery ligation and infarct size in control dogs with mortality and infarct size in dogs previously protected by operation.

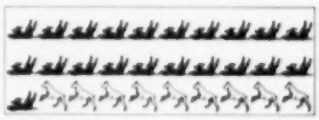
In 30 normal dogs, ligation of the test artery resulted in the death of 70% of the dogs.

BECK I OPERATION
SAVES LIFE AFTER A MAJOR CORONARY ARTERY IS TIED OFF.
TEST ARTERY LIGATED —
DESCENDING RAMUS OF LEFT CORONARY ARTERY.

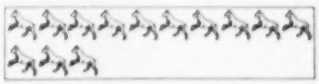
30 DOGS PROTECTED BY BECK I OPERATION
Dead — 26.6%
Living — 73.4%



30 DOGS NOT PROTECTED BY OPERATION
Dead — 70 %
Living — 30 %



SAVED BY OPERATION
13 out of 30 —
43.3 %



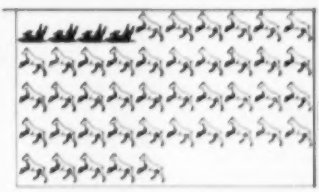
Of 30 dogs protected by the Beck I operation, ligation of the test artery resulted in the death of only 26.6%.

The Beck I operation saved the lives of 13 of the 30 test dogs. The operation also saved myocardium from destruction.

BECK II OPERATION
SAVES LIFE AFTER A MAJOR CORONARY ARTERY IS TIED OFF.
TEST ARTERY LIGATED —
DESCENDING RAMUS OF LEFT CORONARY ARTERY.

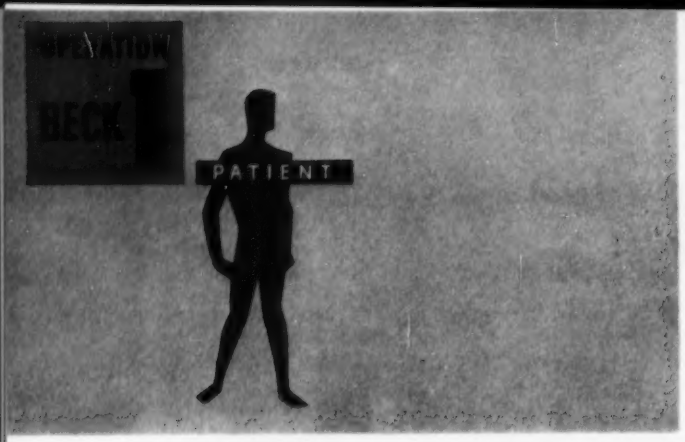
The test of benefit was applied to dogs protected by the Beck II operation. Mortality from descending coronary artery ligation was lowered from 70% in the control dogs to 8.9% in the protected dogs. Operation saved the lives of 27 out of the 45 dogs.

45 DOGS PROTECTED BY BECK II OPERATION
Dead — 8.9%
Living — 91.1%



45 DOGS NOT PROTECTED BY OPERATION
Dead — 70 %
Living — 30 %

SAVED BY OPERATION
27 out of 45 —
60%



The Beck I operation utilizes the following mechanisms of benefit: intercoronary arterial communications, elevation of coronary sinus pressure, and extracoronary communications.

The operative technique is illustrated.

Fig. 8.—Partial ligation coronary sinus. The sinus was ligated to 2 to 3 mm. near its ostium.

Fig. 9.—Abrasion surface of heart. The epicardium was removed by abrasion. The resulting inflammation is a stimulus to the development of intercoronary communications. A raw bed was provided for the tissue graft.

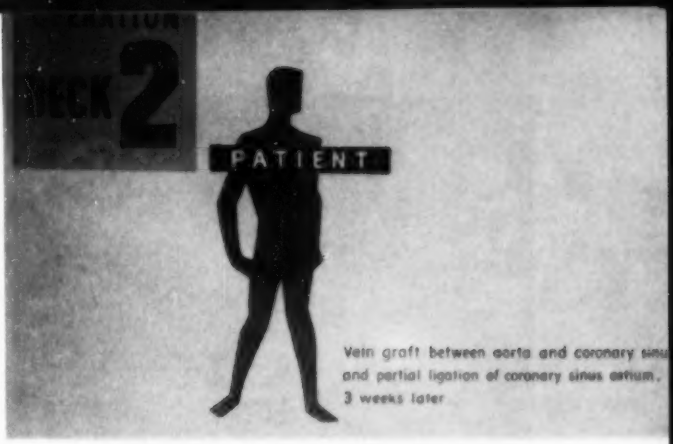
Fig. 10.—Application inflammatory agent (0.2 gm. powdered asbestos). Further inflammation is produced by the application of a mild inflammatory agent, powdered asbestos, to the surface of the heart. This further stimulates the development of intercoronary communications.

Fig. 11.—Parietal pericardium and mediastinal fat grafted to heart. The application of these tissues to the raw surface of the heart provides for the development of extracoronary communications.

The Beck II operation utilizes the following mechanisms of benefit: intercoronary arterial communications, retrograde flow in veins, and elevation of the coronary sinus pressure.

Three weeks after placing the vein graft the sinus is partially ligated to 2 to 3 mm. near its ostium. Ligation of the sinus causes reversal of flow in the veins as demonstrated in the pictures.

The operative technique is illustrated.



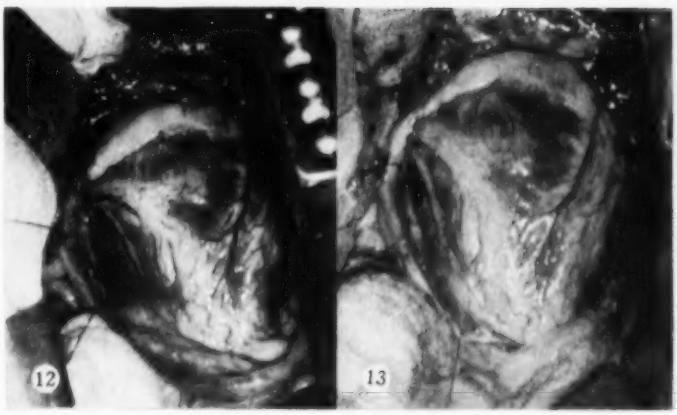


Fig. 12.—Before reversal of flow. Vein graft sutured to coronary sinus, not yet attached to aorta. The arteries show evidence of disease. The veins were blue.

Fig. 13.—After reversal of flow. Vein graft in place between aorta and sinus. Sinus temporarily occluded by traction on sinus ligature. Veins now red and filled with arterial blood.

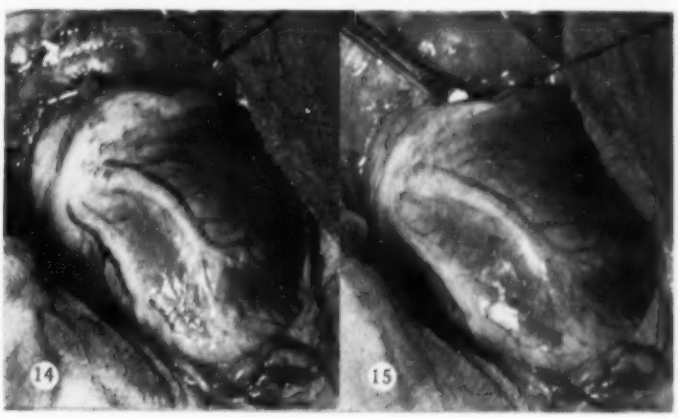
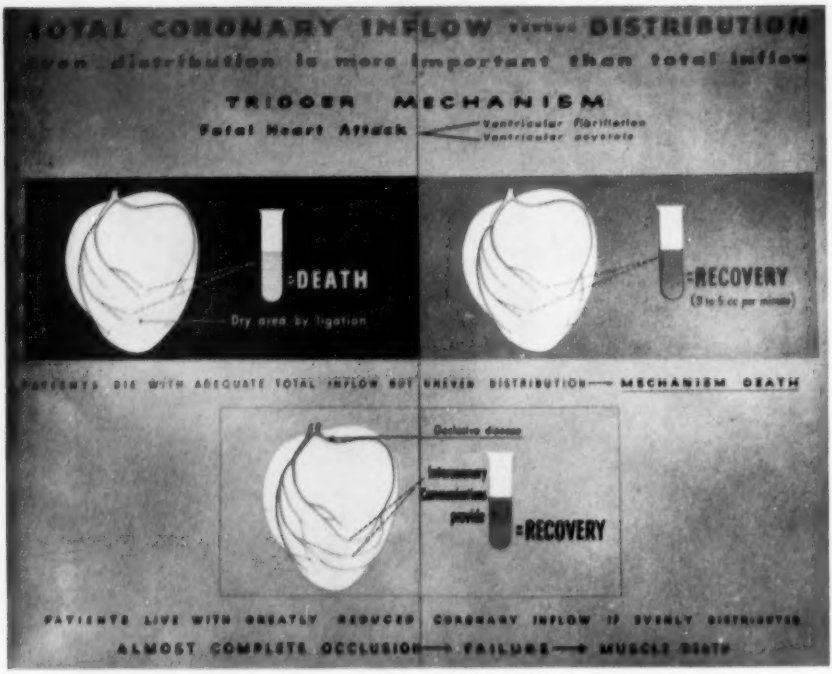


Fig. 14.—Before reversal of flow. Vein graft between aorta and sinus on another patient. The diseased arteries show as white streaks. The veins were blue.

Fig. 15.—After reversal in same heart. Sinus temporarily occluded. The veins were red with arterial blood.


TOTAL CORONARY INFLOW versus DISTRIBUTION
Even distribution is more important than total inflow
TRIGGER MECHANISM
Fatal Heart Attack
Ventricular fibrillation
Ventricular asystole
=DEATH
Dry area by ligation
=RECOVERY
(3 to 5 cc per minute)
PATIENTS DIE WITH ADEQUATE TOTAL INFLOW BUT UNEVEN DISTRIBUTION—MECHANISM DEATH
Occlusive disease
=RECOVERY
PATIENTS LIVE WITH GREATLY REDUCED CORONARY INFLOW IF EVENLY DISTRIBUTED
ALMOST COMPLETE OCCLUSION—FAILURE—MUSCLE DEATH

The blood supply to the myocardium must be considered in terms of distribution of the blood as well as total coronary inflow. With an adequate total coronary inflow death may result from the development of a trigger. A trigger is an ischemic area of myocardium which becomes an ectopic center for impulses from the myocardium and which in turn destroys the coordinated mechanism, resulting in death. This is a mechanism death. About one-third of all deaths due to coronary artery disease are mechanism deaths. This is a large segment of the population. Many of these hearts contain sufficient good myocardium to permit continued function for many years had not the trigger caused death.

Experimental production of a trigger is illustrated by the drawing on the left. A localized area of ischemia was produced by ligation of peripheral arterial twigs. Little or no blood could get into the area, as symbolized by the empty test tube. The area became irritable; the trigger fired, and death from ventricular fibrillation resulted.

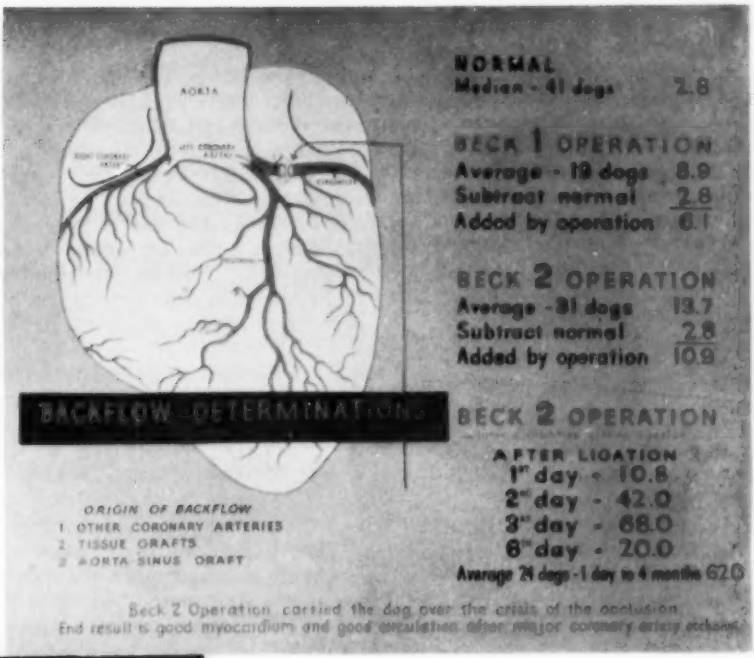
On the right is a drawing of a similar experiment in which several peripheral arterial twigs were not ligated. A trigger did not develop and the heart did not fibrillate. The animal survived. The amount of blood which deactivated the potential trigger was that amount supplied by the unligated arterial twigs, a very small amount of blood, probably no more than 3 to 5 cc. per minute. This small amount of blood which prevented death is symbolized by the test tube containing 5 cc. of blood. In both the above experiments the total coronary inflow was normal.

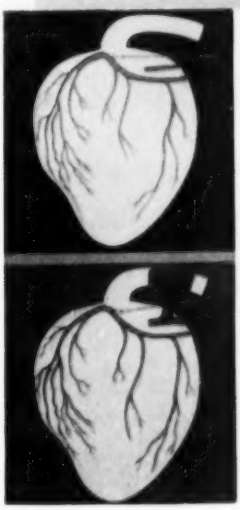
At the bottom is a drawing representing a diseased human heart protected by operation. Occlusive disease has reduced the total coronary inflow. Intercoronary arterial communications provide an even distribution of the blood. A trigger does not develop, and a mechanism death is prevented. The occlusive disease may go on to complete occlusion of the main coronary arteries. The myocardium then gives way to failure, and a muscle type of death results. Operation, by providing intercoronary communications, can supply a small quantity of blood to potential trigger areas so that mechanism death does not develop. Muscle death may eventually develop. By substituting muscle death for mechanism death the operation provides extension of life for the patient, probably in terms of years.

Patients die with adequate total inflow but uneven distribution→mechanism death.

Patients live with greatly reduced coronary inflow if evenly distributed.

Almost complete occlusion→failure →muscle death.


AORTA
BACKFLOW DETERMINATIONS
ORIGIN OF BACKFLOW
1. OTHER CORONARY ARTERIES
2. TISSUE GRAFTS
3. AORTA SINUS GRAFT
NORMAL
Median - 41 dogs 2.8
BECK 1 OPERATION
Average - 19 dogs 8.9
Subtract normal 2.8
Added by operation 6.1
BECK 2 OPERATION
Average - 31 dogs 13.7
Subtract normal 2.8
Added by operation 10.9
BECK 2 OPERATION
AFTER LIGATION
1st day - 10.8
2nd day - 42.0
3rd day - 68.0
6th day - 20.0
Average 24 dogs - 1 day to 4 months 62.0
Beck 2 Operation carried the dog over the crisis of the occlusion.
End result is good myocardium and good circulation after major coronary artery occlusion.



TRIGGER MECHANISM KILLS A LARGE SEGMENT OF POPULATION.

IT IS ACTIVATED BY ANOXIA. Measurements (Eckstein)

CIRCUMFLEX ARTERY LIGATION — death in 1 hour.

20 NORMAL DOGS

Dead 14 — 70%

Living 6 — 30%

CIRCUMFLEX ARTERY LIGATION — death in 1 hour.
RED BLOOD DELIVERED TO CORONARY SINUS AT PRESSURE OF 50 mm.Hg. INCREASES BACKFLOW BY 4cc PER MINUTE FROM 2.8cc. NORMAL TO 68cc. AVERAGE IN 14 DOGS.

20 DOGS

Dead 0 — 0%

Living 20 — 100%

ISCHEMIC AREA — CIRCUMFLEX LIGATION — IS 50% LEFT VENTRICLE
DEACTIVATED BY 4cc. BLOOD PER MINUTE.
SMALLER ISCHEMIC AREAS ARE
DEACTIVATED BY DROPS OR 1 OR 2cc. BLOOD PER MINUTE.

BACKFLOW DETERMINATIONS

The large drawing shows the circumflex artery ligated at its origin. The artery is cut just distal to the ligature. Blood will flow out of the cut distal end of the artery, and the flow is expressed in terms of cubic centimeters per minute. This is the backflow method of Mautz.

Normal

In 41 normal dogs, the median backflow was 2.8 cc. per minute of arterial blood. The source of this blood was the other coronary arteries. Arterial blood entered the other arteries, went across a few small intercoronary communications, and emerged from the cut end of the circumflex artery.

If operation develops additional intercoronary communications, then dogs operated on should show larger than normal backflows.

Beck I operation. The average backflow in 19 dogs operated on was 8.9 cc. per minute. Since 2.8 cc. per minute was normally present, the operation added 6.1 cc. per minute.

The Beck II operation in 31 dogs added 10.9 cc. per minute backflow

blood. These quantities of blood must explain the protection demonstrated in the artery ligation-mortality-infarct tests, shown in Figure 7 and on page 11.

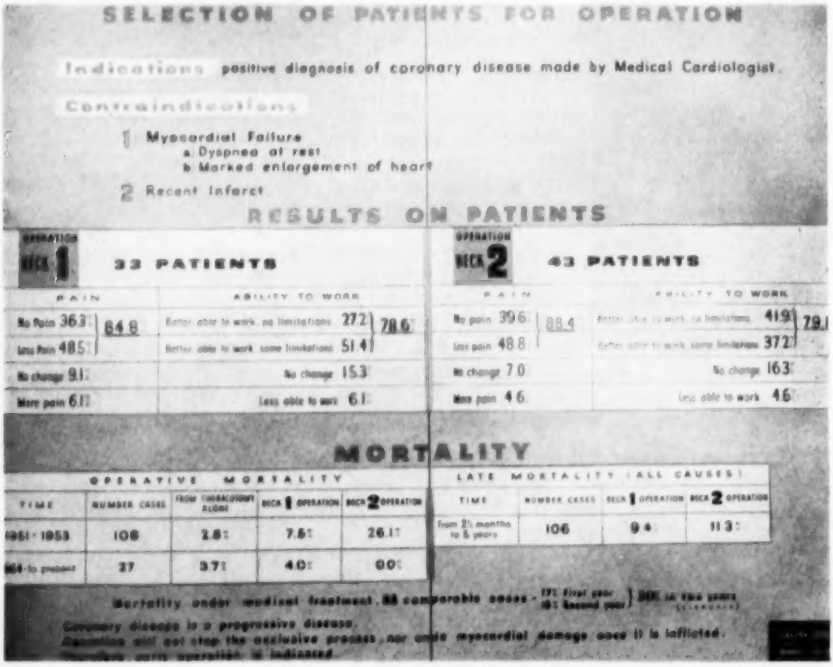
In 24 dogs protected by the Beck II operation in which the circumflex artery was ligated and backflow was studied from 1 day to 4 months following the ligation, the average backflow was 62 cc. per minute. The operation provided these dogs with 10.9 cc. per minute of blood to the circumflex area of myocardium, which prevented death. Because death was prevented, the dogs had time in which additional intercoronary arterial communications developed as the result of the stimulus of artery ligation. The end-result was a good myocardium and good circulation after major coronary artery occlusion.

TRIGGER MECHANISM KILLS A LARGE SEGMENT OF POPULATION

The top drawing illustrates an experiment done by Eckstein. The circumflex artery was ligated at its origin and the dogs observed for one hour. The one-hour mortality in 20 normal dogs was 70%.

In the bottom drawing, the coronary sinus has been acutely arterialized by a Beck II operation. The circumflex artery was ligated at its origin and the dogs observed for one hour. The one-hour mortality in the protected dogs was 0%. Backflow determinations in dogs with acute arterialization of the coronary sinus show an increase in the backflow blood from 2.8 cc. per minute with the graft clamped to 6.8 cc. per minute with the graft open and functioning. The graft, then, added 4 cc. per minute backflow blood. The source of the additional 4 cc. per minute was blood that started as arterial blood in the aorta, went across the graft into the coronary sinus system of veins, and into a capillary bed, where it gave up its oxygen, and then emerged from the cut end of the circumflex artery as venous blood.

The 4 cc. per minute of blood added by the graft must explain the reduction in the one-hour mortality from 70% to 0%. The circumflex area represents about 50% of the mass of the left ventricle, and this ischemic area has been deactivated by 4 cc. of blood per minute. Smaller areas of ischemia, then, may be deactivated by only a few drops of blood per minute.



Patients with so much destruction of myocardium that there is not sufficient remaining myocardium to maintain normal function will not be benefited by operation. Operation cannot restore scar tissue to functional myocardium. Such patients will often exhibit chronic myocardial failure.

Patients with a recent infarct are poor risks for an anesthetic and should not be operated on. Patients are usually advised to wait six months after an infarct before considering operation.

RESULTS ON PATIENTS

Patients were evaluated by comparing their postoperative condition with their preoperative condition. Angina and ability to exercise were considered the most valid criteria. "No pain" means no angina at any time postoperatively. "Less pain" means a marked reduction in frequency and severity of pain, about 70% to 80% reduction. "Better able to work, no limitations" means able to return to their usual occupation with no limitations in activities of any kind. "Better able to work, some limitations" means able to work full time but with some slight limitations to their ability to exercise. Patients were evaluated from three months to about five years postoperatively. The results indicate that four out of five patients are back to work and relatively symptom-free.

MORTALITY

In the three-year period from 1951 through 1953 there were 108 cases operated on. In the first six months of 1954 there were more than 27 cases operated on. The mortality from thoracotomy alone and from the Beck I and the Beck II operations are presented. The late mortality is also presented.

Mortality of comparable cases under standard medical therapy, as reported by Lindgren (*Acta medica scandinavica*, 1950), is also presented. Coronary disease is often a progressive disease. Operation will not stop the occlusive process or undo myocardial damage once it is inflicted.

In order to protect good myocardium against the effects of the progressive occlusive process and prevent the fatal effects of a trigger from developing, operation is advised early, rather than late, in the course of the disease.

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TORSION OF TESTIS IN CASE OF INTERSEXUALITY

K. M. POPOV, M.D., Kragujevac, Yugoslavia

TORSION of the testis in a case of intersexuality is of sufficiently rare occurrence to warrant publication. The present case may fit the category of male pseudohermaphroiditism labeled by Howard [1] as adenoma tubulare and most recently described by Schneider and co-workers [2] in familial form, or it may be an example of true hermaphroiditism.

REPORT OF CASE

A 50-year-old female farmer was sent to the hospital with the diagnosis of incarcerated hernia.

She had never menstruated but had married and had intercourse, without sexual desire. Of great significance is the fact that the patient had three sisters who never menstruated and had not married.

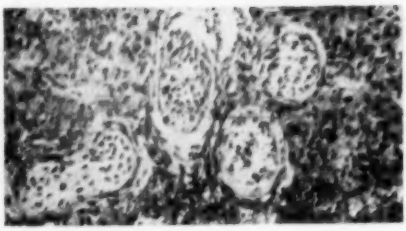
Since childhood the patient had been suffering from a "small hernia" in the right inguinal region, which once, 12 years previously, had become incarcerated, with severe pain, and which subsided after manipulation. In the morning of the day of hospitalization, while hard at work in the fields, the patient suddenly felt a severe pain in the right inguinal region and noted increasing swelling and pain. She was brought to the operating room in shock.

On examination, she appeared to have all the characteristics of the female sex except for flat breasts and male distribution of pubic hair. A large tumor was felt in the right inguinal region, with redness of the overlying skin. The abdomen was distended and tender.

To our surprise, at operation, instead of opening an incarcerated hernial sac, we entered the tunica vaginalis, from which ran 50 cc. of sanguineous fluid. A dark-red testis lay inside, rotated 360 degrees, with an atrophic epididymis floating loose. The mesorchium was strikingly long and thin, and the insertion of the tunica vaginalis was placed high.

The ductus deferens, traced into the abdominal cavity, was found to enter the uterus above the rudimentary tube. On the opposite side a similar abnormality was found. Castration was performed on the damaged side.

On microscopic section (Figure), complete necrosis of testis was seen. In the region of the pyramids, islets of testicular lobules were found, with well-preserved tubular borders and germinal cells. The elastic fibers in the tubules were well stained. Some hemosiderin deposits were noted in the interstitium. The Sertoli cells contained fat droplets, which stained with Sudan III, as did cells in the interstitial tissue. Organized necrotic tissue was seen in some areas, probably as a residual of the torsion which was reduced 12 years before.



Reproduction of photomicrograph showing a few atrophic seminiferous tubules amid sheets of Leydig cells.

COMMENT

No similar case of torsion associated with hermaphroditism could be found in the literature. Whether this is a case of true hermaphroditism or one of male pseudohermaphroditism is not definite. The characteristics of familial undescended male gonads with female external genitalia are typical of the syndrome of adenoma tubulare, a form of male pseudohermaphroditism. In view of the fact that female internal genitalia were found and, biopsy was not performed on the contralateral gonad, it is possible that this case was one of true hermaphroditism.

SUMMARY

Torsion of the testis, associated with intersexuality (male pseudohermaphroditism or true hermaphroditism), is reported.

REFERENCES

1. Howard, F. S.: The Surgery of Intersexuals, J. Urol. **65**:636-649, 1951.

2. Schneider, R. W.; Van Ommen, R. A., and Hoerr, S. O.: Hereditary Occurrence of Testes and Absence of Sexual Hair in Amenorrheic Women: A Type of Pseudohermaphroditism, J. Clin. Endocrinol. **12**:423-438, 1952.

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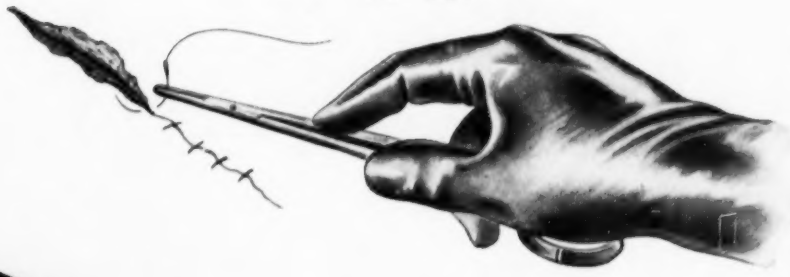

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